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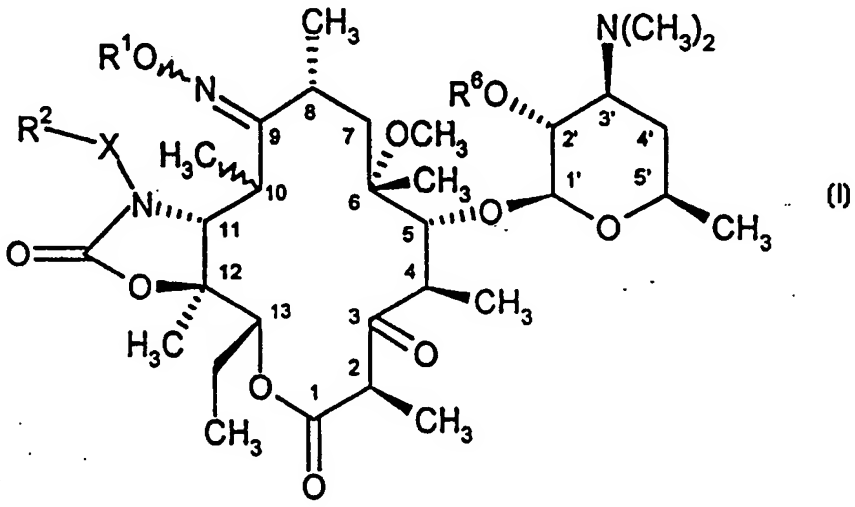

(I)

(57) Abstract

The invention relates to compounds of formula (I), and to pharmaceutically acceptable salts thereof, wherein R^1, R^2, R^6 and X are as defined herein. The invention also relates to pharmaceutical compositions containing the compounds of formula (I), methods of using said compounds of formula (I) in the treatment of bacterial and protozoa infections, and methods of preparing said compounds of formula (I).

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substituted by 1 to 4 substituents, and the nitrogen atom where X^1 is -NH- is optionally substituted by 1 substituent, said optional substituents being independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, -NR^7R^8, C_6-C_{10} aryl, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$;

R^1 is H or C_1-C_{10} alkyl, wherein 1 to 3 carbons of said alkyl are optionally replaced by a heteroatom selected from O, S and N, and said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, -NR^7R^8, C_6-C_{10} aryl, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$;

R^2 is (i) H, R^4, -C(O)R^4, -C(O)OR^4 or -$(CR^7R^8)_mR^3$ when X is -NR^7-, or (ii) H, R^4, or -$(CR^7R^8)_mR^3$ when X is -CR^7R^8-, wherein for both (i) and (ii) m is an integer ranging from 0 to 6 and both R^7 and R^8 may vary for each iteration where m is greater than 1;

each R^3 is independently C_6-C_{10} aryl or 5-10 membered heterocyclyl, wherein said aryl and heterocyclyl groups are optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_6-C_{10} aryl, C_1-C_{10} alkyl, -NR^7R^8, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$; and,

each R^4 and R^5 is independently selected from H and C_1-C_{12} alkyl wherein one or two carbons of said alkyl are optionally replaced by a heteroatom selected from O, S and N, and wherein said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, C_1-C_{10} alkyl, -NR^7R^8, C_6-C_{10} aryl, 5-10 membered heterocyclyl, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$;

R^6 is H, -C(O)R^3 or C_1-C_{18} alkanoyl, wherein in the alkyl portion of said alkanoyl one or two carbons optionally may be replaced by a heteroatom selected from O, S and N; and,

each R^7 and R^8 is independently H or C_1-C_6 alkyl.

More specific embodiments of this invention include compounds of formula I wherein R^6 is H.

Other more specific embodiments of this invention include compounds of formula I wherein X is -NH-.

Other more specific embodiments of this invention include compounds of formula I wherein R^1 is H, benzyl or C_1-C_3 alkyl or -$CH_2O(CH_2)_2OCH_3$.

Other more specific embodiments of this invention include compounds of formula I wherein R^2 is -$(CH_2)_mR^3$ wherein m is an integer ranging from 0 to 6 and R^3 is 5-10 membered

heterocyclyl or C_6-C_{10} aryl. Specific embodiments of R^3 include quinolin-4-yl, 4-phenyl-imidazol-1-yl, imidazo(4,5-b)pyridin-3-yl, 4-pyridin-3-ylimidazol-1-yl and pyridin-3-yl.

Examples of preferred compounds of this invention include:

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-pyridin-3-yl-imidazol-1-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-pyridin-3-yl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(imidazo(4,5-b)pyridin-3-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(imidazo(4,5-b)pyridin-3-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(7-methoxy-quinolin-4-yl)-propyl))hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(7-methoxy-quinolin-4-yl)-propyl))hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-benzoimidazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-benzoimidazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-carbazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-carbazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(5-phenyl-1H-pyrrol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(5-phenyl-1H-pyrrol-2-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-chlorophenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-chlorophenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-(3-(4-methoxyphenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-(3-(4-methoxyphenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-pyridin-4-yl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-pyridin-4-yl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-naphthalen-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-naphthalen-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(1H-indol-3-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(1H-indol-3-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-4-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-4-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-3-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-3-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(pyridin-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(pyridin-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-phenylpropyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-phenylpropyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-bis-(3-phenylpropyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-bis-(3-phenylpropyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-hydroxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-hydroxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(2-phenylethyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(2-phenylethyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(4-phenylbutyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(4-phenylbutyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-furan-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-furan-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-thiophen-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-thiophen-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrrol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrrol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-pyridin-3-yl-thiazol-4-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-pyridin-3-yl-thiazol-4-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-phenyl-thiazol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-phenyl-thiazol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-1H-imidazol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-1H-imidazol-2-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate; and the pharmaceutically acceptable salts of the foregoing compounds.

The invention also relates to a pharmaceutical composition for the treatment of a bacterial infection or a protozoa infection in a mammal, fish, or bird which comprises a therapeutically effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The invention also relates to a method of treating a bacterial infection or a protozoa infection in a mammal, fish, or bird which comprises administering to said mammal, fish or bird a therapeutically effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof.

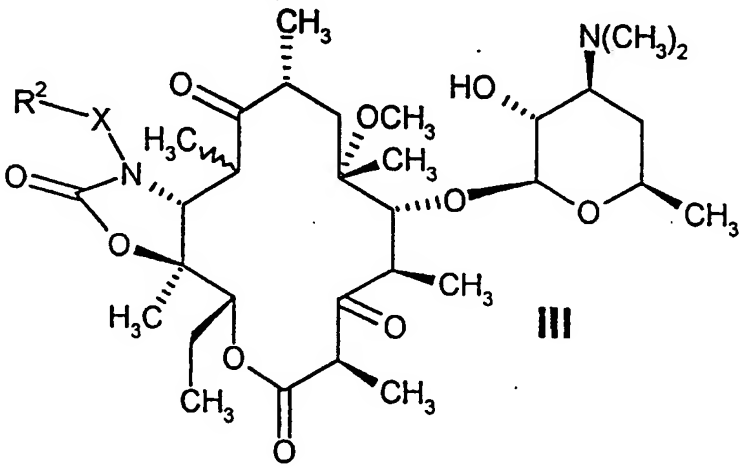
The term "treatment", as used herein, unless otherwise indicated, includes the treatment or prevention of a bacterial infection or protozoa infection as provided in the method of the present invention.

As used herein, unless otherwise indicated, the term "bacterial infection(s)" or "protozoa infection" includes bacterial infections and protozoa infections that occur in mammals, fish and birds as well as disorders related to bacterial infections and protozoa infections that may be treated or prevented by administering antibiotics such as the compounds of the present invention. Such bacterial infections and protozoa infections and disorders related to such infections include the following: pneumonia, otitis media, sinusitus, bronchitis, tonsillitis, and mastoiditis related to infection by *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Staphylococcus aureus,* or *Peptostreptococcus* spp.; pharyngitis, rheumatic fever, and glomerulonephritis related to infection by *Streptococcus pyogenes,* Groups C and G streptococci, *Clostridium diptheriae,* or *Actinobacillus haemolyticum;* respiratory tract infections related to infection by *Mycoplasma pneumoniae, Legionella pneumophila, Streptococcus pneumoniae, Haemophilus influenzae,* or *Chlamydia pneumoniae;* uncomplicated skin and soft tissue infections, abscesses and osteomyelitis, and puerperal fever related to

infection by *Staphylococcus aureus*, coagulase-positive staphylococci (i.e., *S. epidermidis, S. hemolyticus*, etc.), *Streptococcus pyogenes , Streptococcus agalactiae*, Streptococcal groups C-F (minute-colony streptococci), viridans streptococci, *Corynebacterium minutissimum, Clostridium* spp., or *Bartonella henselae;* uncomplicated acute urinary tract infections related to infection by *Staphylococcus saprophyticus* or *Enterococcus* spp.; urethritis and cervicitis; and sexually transmitted diseases related to infection by *Chlamydia trachomatis, Haemophilus ducreyi, Treponema pallidum, Ureaplasma urealyticum,* or *Neiserria gonorrheae;* toxin diseases related to infection by *S. aureus* (food poisoning and Toxic shock syndrome), or Groups A, B, and C streptococci; ulcers related to infection by *Helicobacter pylori;* systemic febrile syndromes related to infection by *Borrelia recurrentis;* Lyme disease related to infection by *Borrelia burgdorferi;* conjunctivitis, keratitis, and dacrocystitis related to infection by *Chlamydia trachomatis, Neisseria gonorrhoeae, S. aureus, S. pneumoniae, S. pyogenes, H. influenzae,* or *Listeria* spp.; disseminated *Mycobacterium avium* complex (MAC) disease related to infection by *Mycobacterium avium,* or *Mycobacterium intracellulare;* gastroenteritis related to infection by *Campylobacter jejuni;* intestinal protozoa related to infection by *Cryptosporidium* spp.; odontogenic infection related to infection by viridans streptococci; persistent cough related to infection by *Bordetella pertussis;* gas gangrene related to infection by *Clostridium perfringens* or *Bacteroides* spp.; and atherosclerosis related to infection by *Helicobacter pylori* or *Chlamydia pneumoniae.* Bacterial infections and protozoa infections and disorders related to such infections that may be treated or prevented in animals include the following: bovine respiratory disease related to infection by *P. haem., P. multocida, Mycoplasma bovis,* or *Bordetella* spp.; cow enteric disease related to infection by *E. coli* or protozoa (i.e., coccidia, cryptosporidia, etc.); dairy cow mastitis related to infection by *Staph. aureus, Strep. uberis, Strep. agalactiae, Strep. dysgalactiae, Klebsiella* spp., *Corynebacterium,* or *Enterococcus* spp.; swine respiratory disease related to infection by *A. pleuro., P. multocida,* or *Mycoplasma* spp.; swine enteric disease related to infection by *E. coli, Lawsonia intracellularis, Salmonella,* or *Serpulina hyodyisinteriae;* cow footrot related to infection by *Fusobacterium* spp.; cow metritis related to infection by *E. coli;* cow hairy warts related to infection by *Fusobacterium necrophorum* or *Bacteroides nodosus;* cow pink-eye related to infection by *Moraxella bovis;* cow premature abortion related to infection by protozoa (i.e. neosporium); urinary tract infection in dogs and cats related to infection by *E. coli;* skin and soft tissue infections in dogs and cats related to infection by *Staph. epidermidis, Staph. intermedius, coagulase neg. Staph.* or *P. multocida;* and dental or mouth infections in dogs and cats related to infection by *Alcaligenes* spp., *Bacteroides* spp., *Clostridium* spp., *Enterobacter* spp., *Eubacterium, Peptostreptococcus, Porphyromonas,* or *Prevotella.* Other bacterial infections and protozoa infections and disorders related to such infections that may be treated or prevented in accord with the method of the present invention are referred to in

J. P. Sanford et al., "The Sanford Guide To Antimicrobial Therapy," 26th Edition, (Antimicrobial Therapy, Inc., 1996).

The invention also relates to a process of preparing the compound of formula I, and pharmaceutically acceptable salts thereof, wherein R^1, R^2, R^6 and X are as defined above, which comprises treating a compound of the formula



III

wherein X and R^2 are as defined above, with a compound of the formula $R^1ONH_2 \cdot HCl$ or R^1ONH_2, wherein R^1 is as defined for said compound of formula I, in the presence of an acid, in a polar solvent such as methanol, ethanol, or isopropyl alcohol. Preferably, said acid is Py•HCl, wherein Py denotes pyridine, or $Et_3N \cdot HCl$.

In the chemical structures depicted herein, a wavy line indicates that the stereochemistry at the chiral center to which the wavy line is connected is either an R or S configuration where the wavy line is connected to a carbon atom. In the compound of formula I, the wavy line at position 10 of the macrolide ring indicates that the methyl group can be either R or S configuration at that position. In the compound of formula I, the wavy line connected to the oxime nitrogen at position 9 of the macrolide ring indicates that the $-OR^1$ moiety is in an E or Z configuration.

The term "halo", as used herein, unless otherwise indicated, means fluoro, chloro, bromo or iodo. Preferred halo groups are fluoro, chloro and bromo.

The term "alkyl", as used herein, unless otherwise indicated, includes saturated monovalent hydrocarbon radicals having straight, cyclic or branched moieties, or mixtures thereof. Said alkyl group may include one or two double or triple bonds. It is understood that for cyclic moieties at least three carbon atoms are required in said alkyl group.

The term "alkanoyl", as used herein, unless otherwise indicated, includes -C(O)-alkyl groups wherein "alkyl" is as defined above.

The term "aryl", as used herein, unless otherwise indicated, includes an organic radical derived from an aromatic hydrocarbon by removal of one hydrogen, such as phenyl or naphthyl.

The term "5-10 membered heterocyclyl", as used herein, unless otherwise indicated, includes aromatic and non-aromatic heterocyclic groups containing one or more heteroatoms each selected from O, S and N, wherein each heterocyclic group has from 5-10 atoms in its ring system. The heterocyclic groups include benzo-fused ring systems and ring systems substituted with one or more oxo moieties. An example of a 5 membered heterocyclic group is thiazolyl, and an example of a 10 membered heterocyclic group is quinolinyl. Examples of non-aromatic heterocyclic groups are pyrrolidinyl, piperidino, morpholino, thiomorpholino and piperazinyl. Examples of aromatic heterocyclic groups are pyridinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, tetrazolyl, furyl, thienyl, isoxazolyl and thiazolyl. Heterocyclic groups having a fused benzene ring include benzimidazolyl.

The phrase "pharmaceutically acceptable salt(s)", as used herein, unless otherwise indicated, includes salts of acidic or basic groups which may be present in the compounds of formula I. The compounds of formula I that are basic in nature are capable of forming a wide variety of salts with various inorganic and organic acids. The acids that may be used to prepare pharmaceutically acceptable acid addition salts of such basic compounds of formula I are those that form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, phosphate, acid phosphate, isonicotinate, acetate, lactate, salicylate, citrate, acid citrate, tartrate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucaronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate [i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)] salts.

Those compounds of the formula I that are acidic in nature, are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline earth metal salts and particularly, the sodium and potassium salts.

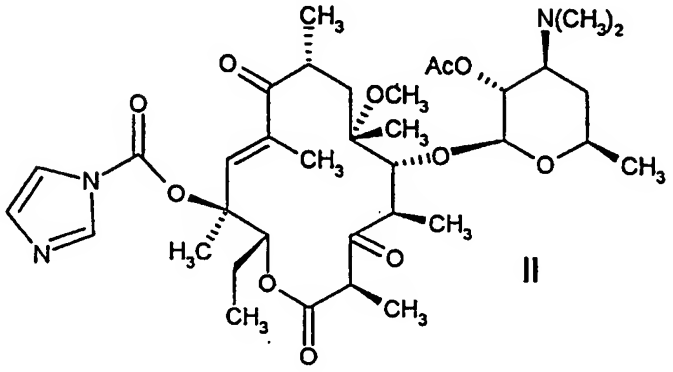
The present invention also includes all radiolabelled forms of the compounds of formula I, and pharmaceutically acceptable salts thereof, wherein the radiolabel is selected from ^{3}H, ^{11}C and ^{14}C. Such radiolabelled compounds are useful as research or diagnostic tools.

Certain compounds of formula I may have asymmetric centers and therefore exist in different enantiomeric forms. This invention relates to the use of all optical isomers and stereoisomers of the compounds of formula I and mixtures thereof. In particular, the invention includes both the R and S configurations of the methyl group at C-10 of the macrolide ring of formula I, and both the E and Z configurations of the $-OR^1$ group connected to the nitrogen of the oxime molety at C-9 of the macrolide ring of formula I. The compounds of formula I may also exist as tautomers. This invention relates to the use of all such tautomers and mixtures thereof.

Detailed Description of the Invention

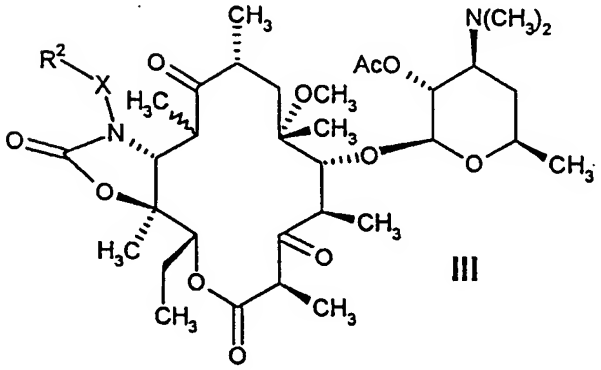
The preparation of the compounds of the present invention is illustrated in the following Schemes.

Scheme 1



II

1

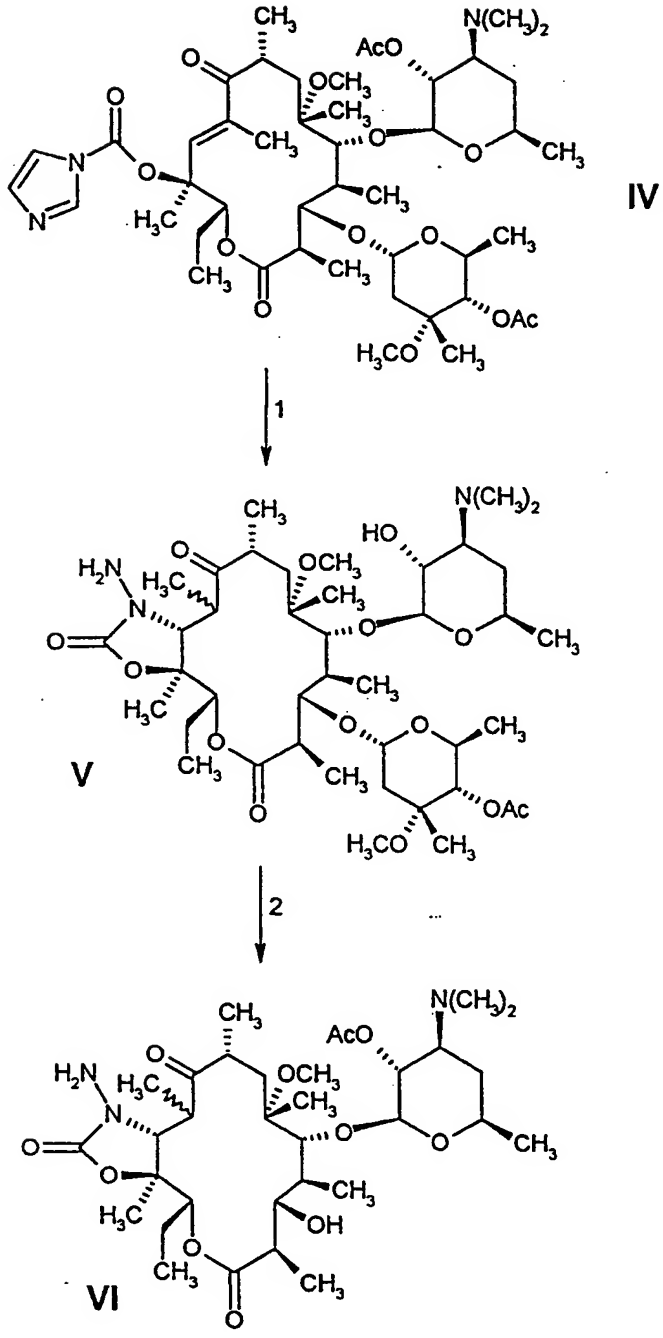


III

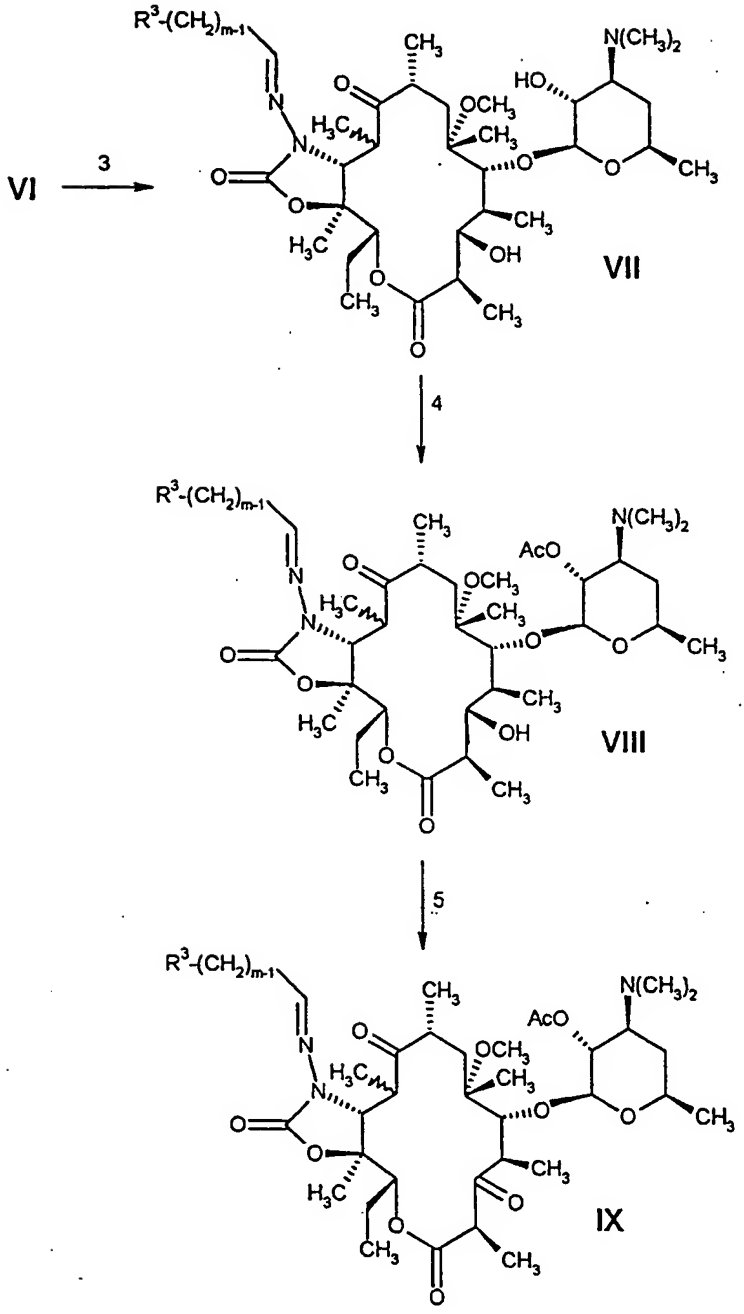
2

I

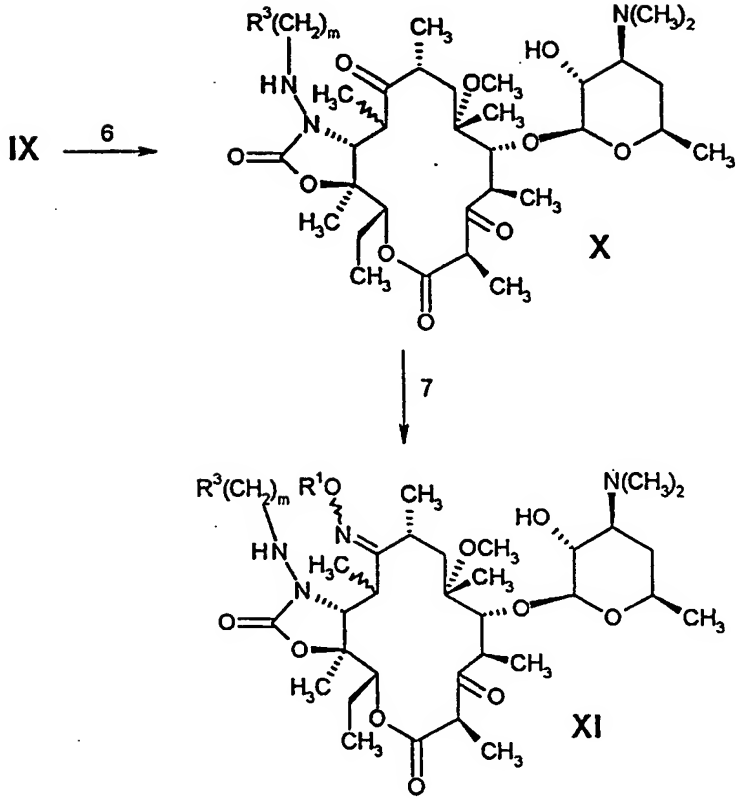
Scheme 2



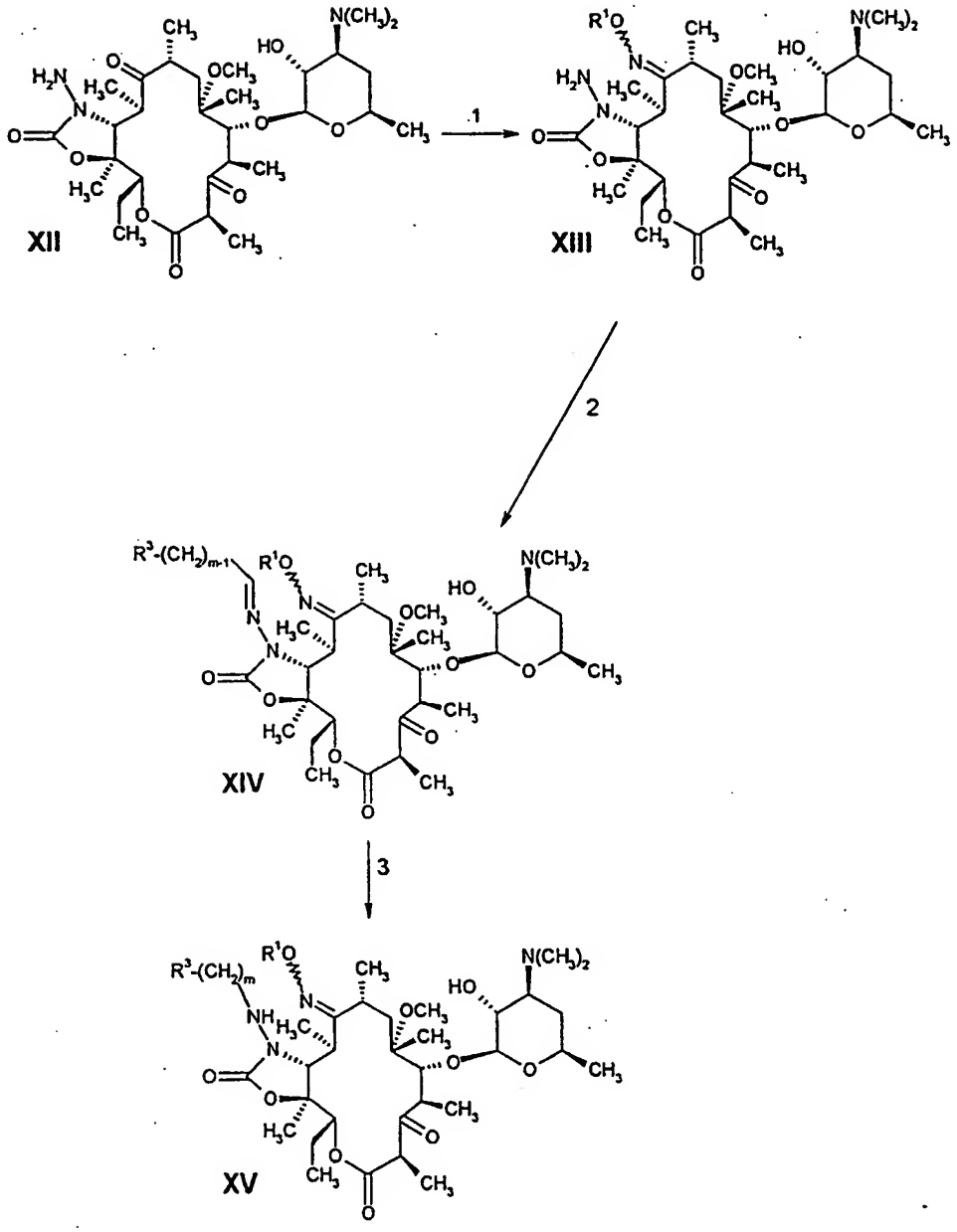
Scheme 2 continued



Scheme 2 continued



Scheme 3



In the above Schemes, "Ac" indicates an acetyl group. The compounds of the present invention are readily prepared. Scheme 1 illustrates the general synthesis of the compounds of the present invention. In Scheme 1, the starting compound of formula II can be prepared as described in United States patent 5,543,400 (issued August 6, 1996). In general, the intermediate compound of formula III can be prepared as described in United States patent 5,543,400, referred to above, United States patent 5,527,780 (issued June 18, 1996), United Kingdom patent application number 2,288,174 (published October 11, 1995), and G. Griesgraber *et al.*, "3-Keto-11,12-carbazate Derivatives of 6-O-Methylerythromycin A," Journal of Antibiotics, 49(5), 465-477 (1996).

In step 1 of Scheme 1, compounds of the formula III, wherein X is $-CR^7R^8-$ and R^2 is as defined above, can be prepared by treating a compound of the formula II with a compound of the formula $H_2N\text{-}X\text{-}R^2$, wherein X and R^2 are as indicated for said compound of formula III, in a solvent such as acetonitrile, dimethylformamide (DMF), tetrahydrofuran (THF), dimethoxy ethane or dimethylsulfoxide (DMSO), at a temperature within the range of about 50°C to 90°C for a period of about 4 to 10 hours. The preparation of compounds of the formula III wherein X is $-CR^7R^8-$ is described in further detail in United States patents 5,543,400 and 5,527,780, referred to above. Compounds of the formula III, wherein X is -NH- and R^2 is as defined above, can be prepared by treating a compound of the formula II with a compound of the formula H_2NNHR^2, wherein R^2 is as defined above, in a solvent such as acetonitrile, dioxane, or DMSO, at a temperature within the range of about 40°C to 90°C for a period of about 12 hours. The preparation of the compound of formula III wherein X is -NH- is described in further detail in United Kingdom patent application number 2,288,174, referred to above. In step 2 of Scheme 1, compounds of the formula I can be prepared by treating a compound of the formula III with a compound of the formula $R^1ONH_2{\cdot}HCl$ or R^1ONH_2, wherein R^1 is as defined above, in the presence of an acid, such as Py•HCl, wherein Py denotes pyridine, or $Et_3N{\cdot}HCl$, in a polar solvent, preferably methanol, ethanol, or isopropyl alcohol, at a temperature within the range of about 65°C to 95°C for a period of about 10 hours to 6 days.

Scheme 2 illustrates an alternative method of preparing compounds of the formula I wherein X is -NH-. In Scheme 2, the compound of formula IV can be prepared according to the procedures described in Baker *et al.*, Journal of Organic Chemistry, 53, 2340 (1988). In step 1 of Scheme 2, the compound of formula V can be prepared by treating the compound of formula IV with hydrazine according to the procedure described above for the preparation of the compound of formula III wherein X is -NH-. Preferably, the compound of formula V is prepared by treating a compound of formula IV with anhydrous hydrazine in a solvent such as MeCN or DMF at a temperature of from about 60°C to 90°C for about 12 hours. In step 2 of Scheme 2, the compound of formula VI can be prepared by treating a compound of formula V with an acid, such as hydrochloric acid, in a solvent such as methanol or ethanol. In step 3 of Scheme 2, the

compound of formula VII can be prepared by treating a compound of formula VI with a compound of the formula R^3-$(CH_2)_{m-1}$-C(O)H, wherein m is 1 to 7 and R^3 is as defined above, in an anhydrous solvent, such as anhydrous ethanol or isopropanol, at a temperature within the range of about 80°C to 90°C.

In steps 4 and 5 of Scheme 2, the hydroxy group at position C-2' of the compound of formula VII is protected as an acetate by treating the compound with acetic anhydride to form the compound of formula VIII, followed by oxidation of the hydroxy group at position 3 to provide a carbonyl group. Preferably, this is done by treating the compound of formula VII with acetic anhydride in a solvent such as CH_2Cl_2 at ambient temperature to provide the compound of formula VIII. The compound of formula IX can be prepared by treating a compound of formula VIII, in a solvent such as CH_2Cl_2, with DMSO, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDAC) and pyridinium trifluoroacetate (Py•TFA) at ambient temperature. The compound of formula X can be prepared by treating the compound of formula IX with a reducing agent such as $NaBH_3CN$ in a solvent such as methanol at ambient temperature. The compound of formula XI can be prepared as described above for step 2 of Scheme 1.

Scheme 3 illustrates an additional method of preparing compounds of the formula I wherein X is -NH-. In Scheme 3, the compound of formula XII can be prepared according to the procedures described in Griesgraber *et al.*, Journal of Antibiotics, 49(5), 465-477 (1966). In step 1 of Scheme 3, the compound of formula XII can be prepared by treating the compound of formula XII with a compound of the formula R^1ONH_2•HCl or R^1ONH_2 in the presence of an acid such as Py•HCl, wherein Py denotes pyridine, or Et_3N•HCl, in a polar solvent, preferably ethanol, methanol, or isopropyl alcohol, at a temperature within the range of about 65°C to 95°C for a period of about 10 hours to 4 days. In step 2 of Scheme 3, the compound of formula XIII can be converted to the compound of formula XIV according to the procedure of step 3 of Scheme 2. In step 3 of Scheme 3, the compound of formula XIV can be converted to the compound of formula XV according to the procedure of step 6 of Scheme 2.

The compounds of the present invention may have asymmetric carbon atoms. Such diasteromeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods known to those skilled in the art, for example, by chromatography or fractional crystallization. Enantiomers can be separated by converting the enantiomeric mixtures into a diastereomric mixture by reaction with an appropriate optically active compound (e.g., alcohol), separating the diastereomers and converting (e.g., hydrolyzing) the individual diastereomers to the corresponding pure enantiomers. All such isomers, including diastereomer mixtures and pure enantiomers are considered as part of the invention.

The compounds of formula I that are basic in nature are capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to

initially isolate the compound of formula I from the reaction mixture as a pharmaceutically unacceptable salt and then simply convert the latter back to the free base compound by treatment with an alkaline reagent and subsequently convert the latter free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the base compounds of this invention are readily prepared by treating the base compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent medium or in a suitable organic solvent, such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is readily obtained. The desired acid salt can also be precipitated from a solution of the free base in an organic solvent by adding to the solution an appropriate mineral or organic acid.

Those compounds of the formula I that are acidic in nature, are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline-earth metal salts and particularly, the sodium and potassium salts. These salts may be prepared by conventional techniques. The chemical bases which are used as reagents to prepare the pharmaceutically acceptable base salts of this invention are those which form non-toxic base salts with the acidic compounds of formula I. Such non-toxic base salts include those derived from such pharmacologically acceptable cations as sodium, potassium calcium and magnesium, etc. These salts can be prepared by treating the corresponding acidic compounds with an aqueous solution containing the desired pharmacologically acceptable cations, and then evaporating the resulting solution to dryness, preferably under reduced pressure. Alternatively, they may also be prepared by mixing lower alkanolic solutions of the acidic compounds and the desired alkali metal alkoxide together, and then evaporating the resulting solution to dryness in the same manner as before. In either case, stoichiometric quantities of reagents are preferably employed in order to ensure completeness of reaction and maximum yields of the desired final product.

The activity of the compounds of the present invention against bacterial and protozoa pathogens is demonstrated by the compound's ability to inhibit growth of defined strains of human (Assay I) or animal (Assays II and III) pathogens.

Assay I

Assay I, described below, employs conventional methodology and interpretation criteria and is designed to provide direction for chemical modifications that may lead to compounds that circumvent defined mechanisms of macrolide resistance. In Assay I, a panel of bacterial strains is assembled to include a variety of target pathogenic species, including representatives of macrolide resistance mechanisms that have been characterized. Use of this panel enables the chemical structure/activity relationship to be determined with respect to potency, spectrum of activity, and structural elements or modifications that may be necessary to obviate resistance mechanisms. Bacterial pathogens that comprise the screening panel are shown in the table

below. In many cases, both the macrolide-susceptible parent strain and the macrolide-resistant strain derived from it are available to provide a more accurate assessment of the compound's ability to circumvent the resistance mechanism. Strains that contain the gene with the designation of *ermA/ermB/ermC* are resistant to macrolides, lincosamides, and streptogramin B antibiotics due to modifications (methylation) of 23S rRNA molecules by an Erm methylase, thereby generally prevent the binding of all three structural classes. Two types of macrolide efflux have been described; *msrA* encodes a component of an efflux system in staphylococci that prevents the entry of macrolides and streptogramins while *mefA/E* encodes a transmembrane protein that appears to efflux only macrolides. Inactivation of macrolide antibiotics can occur and can be mediated by either a phosphorylation of the 2'-hydroxyl (*mph*) or by cleavage of the macrocyclic lactone (esterase). The strains may be characterized using conventional polymerase chain reaction (PCR) technology and/or by sequencing the resistance determinant. The use of PCR technology in this application is described in J. Sutcliffe et al., "Detection Of Erythromycin-Resistant Determinants By PCR", Antimicrobial Agents and Chemotherapy, 40(11), 2562-2566 (1996). The assay is performed in microtiter trays and interpreted according to Performance Standards for Antimicrobial Disk Susceptibility Tests - Sixth Edition; Approved Standard, published by The National Committee for Clinical Laboratory Standards (NCCLS) guidelines; the minimum inhibitory concentration (MIC) is used to compare strains. Compounds are initially dissolved in dimethylsulfoxide (DMSO) as 40 mg/ml stock solutions.

Strain Designation	Macrolide Resistance Mechanism(s)
Staphylococcus aureus 1116	susceptible parent
Staphylococcus aureus 1117	ermB
Staphylococcus aureus 0052	susceptible parent
Staphylococcus aureus 1120	ermC
Staphylococcus aureus 1032	msrA, mph, esterase
Staphylococcus hemolyticus 1006	msrA, mph
Streptococcus pyogenes 0203	susceptible parent
Streptococcus pyogenes 1079	ermB
Streptococcus pyogenes 1062	susceptible parent
Streptococcus pyogenes 1061	ermB
Streptococcus pyogenes 1064	ermB
Streptococcus agalactiae 1024	susceptible parent
Streptococcus agalactiae 1023	ermB
Streptococcus pneumoniae 1016	susceptible

Streptococcus pneumoniae 1046	ermB
Streptococcus pneumoniae 1095	ermB
Streptococcus pneumoniae 1175	mefE
Streptococcus pneumoniae 0085	susceptible
Haemophilus influenzae 0131	susceptible
Moraxella catarrhalis 0040	susceptible
Moraxella catarrhalis 1055	erythromycin intermediate resistance
Escherichia coli 0266	susceptible

Assay II is utilized to test for activity against *Pasteurella multocida* and Assay III is utilized to test for activity against *Pasteurella haemolytica*.

Assay II

This assay is based on the liquid dilution method in microliter format. A single colony of *P. multocida* (strain 59A067) is inoculated into 5 ml of brain heart infusion (BHI) broth. The test compounds are prepared by solubilizing 1 mg of the compound in 125 µl of dimethylsulfoxide (DMSO). Dilutions of the test compound are prepared using uninoculated BHI broth. The concentrations of the test compound used range from 200 µg/ml to 0.098 µg/ml by two-fold serial dilutions. The *P. multocida* inoculated BHI is diluted with uninoculated BHI broth to make a 10^4 cell suspension per 200 µl. The BHI cell suspensions are mixed with respective serial dilutions of the test compound, and incubated at 37°C for 18 hours. The minimum inhibitory concentration (MIC) is equal to the concentration of the compound exhibiting 100% inhibition of growth of P. multocida as determined by comparison with an uninoculated control.

Assay III

This assay is based on the agar dilution method using a Steers Replicator. Two to five colonies isolated from an agar plate are inoculated into BHI broth and incubated overnight at 37°C with shaking (200 rpm). The next morning, 300 µl of the fully grown *P. haemolytica* preculture is inoculated into 3 ml of fresh BHI broth and is incubated at 37°C with shaking (200 rpm). The appropriate amounts of the test compounds are dissolved in ethanol and a series of two-fold serial dilutions are prepared. Two ml of the respective serial dilution is mixed with 18 ml of molten BHI agar and solidified. When the inoculated *P. haemolytica* culture reaches 0.5 McFarland standard density, about 5 µl of the *P. haemolytica* culture is inoculated onto BHI agar plates containing the various concentrations of the test compound using a Steers Replicator and incubated for 18 hours at 37°C. Initial concentrations of the test compound range from 100-200 µg/ml. The MIC is equal to the concentration of the test compound exhibiting 100% inhibition of growth of *P. haemolytica* as determined by comparison with an uninoculated control.

The in vivo activity of the compounds of formula (I) can be determined by conventional animal protection studies well known to those skilled in the art, usually carried out in mice.

Mice are allotted to cages (10 per cage) upon their arrival, and allowed to acclimate for a minimum of 48 hours before being used. Animals are inoculated with 0.5 ml of a 3×10^3 CFU/ml bacterial suspension (*P. multocida* strain 59A006) intraperitoneally. Each experiment has at least 3 non-medicated control groups including one infected with 0.1X challenge dose and two infected with 1X challenge dose; a 10X challenge data group may also be used. Generally, all mice in a given study can be challenged within 30-90 minutes, especially if a repeating syringe (such as a Cornwall® syringe) is used to administer the challenge. Thirty minutes after challenging has begun, the first compound treatment is given. It may be necessary for a second person to begin compound dosing if all of the animals have not been challenged at the end of 30 minutes. The routes of administration are subcutaneous or oral doses. Subcutaneous doses are administered into the loose skin in the back of the neck whereas oral doses are given by means of a feeding needle. In both cases, a volume of 0.2 ml is used per mouse. Compounds are administered 30 minutes, 4 hours, and 24 hours after challenge. A control compound of known efficacy administered by the same route is included in each test. Animals are observed daily, and the number of survivors in each group is recorded. The *P. multocida* model monitoring continues for 96 hours (four days) post challenge.

The PD_{50} is a calculated dose at which the compound tested protects 50% of a group of mice from mortality due to the bacterial infection which would be lethal in the absence of drug treatment.

The compounds of formula I, and the pharmaceutically acceptable salts thereof (hereinafter "the active compounds"), may be adminstered through oral, parenteral, topical, or rectal routes in the treatment or prevention of bacterial or protozoa infections. In general, these compounds are most desirably administered in dosages ranging from about 0.2 mg per kg body weight per day (mg/kg/day) to about 200 mg/kg/day in single or divided doses (i.e., from 1 to 4 doses per day), although variations will necessarily occur depending upon the species, weight and condition of the subject being treated and the particular route of administration chosen. However, a dosage level that is in the range of about 4 mg/kg/day to about 50 mg/kg/day is most desirably employed. Variations may nevertheless occur depending upon the species of mammal, fish or bird being treated and its individual response to said medicament, as well as on the type of pharmaceutical formulation chosen and the time period and interval at which such administration is carried out. In some instances, dosage levels below the lower limit of the aforesaid range may be more than adequate, while in other cases still larger doses may be employed without causing any harmful side effects, provided that such larger doses are first divided into several small doses for administration throughout the day.

The active compounds may be administered alone or in combination with pharmaceutically acceptable carriers or diluents by the routes previously indicated, and such administration may be carried out in single or multiple doses. More particularly, the active compounds may be administered in a wide variety of different dosage forms, i.e., they may be combined with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, salves, suppositories, jellies, gels, pastes, lotions, ointments, aqueous suspensions, injectable solutions, elixirs, syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various non-toxic organic solvents, etc. Moreover, oral pharmaceutical compositions can be suitably sweetened and/or flavored. In general, the active compounds are present in such dosage forms at concentration levels ranging from about 5.0% to about 70% by weight.

For oral administration, tablets containing various excipients such as microcrystalline cellulose, sodium citrate, calcium carbonate, dicalcium phosphate and glycine may be employed along with various disintegrants such as starch (and preferably corn, potato or tapioca starch), alginic acid and certain complex silicates, together with granulation binders like polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes. Solid compositions of a similar type may also be employed as fillers in gelatin capsules; preferred materials in this connection also include lactose or milk sugar as well as high molecular weight polyethylene glycols. When aqueous suspensions and/or elixirs are desired for oral adinistration, the active compound may be combined with various sweetening or flavoring agents, coloring matter or dyes, and, if so desired, emulsifying and/or suspending agents as well, together with such diluents as water, ethanol, propylene glycol, glycerin and various like combinations thereof.

For parenteral administration, solutions of an active compound in either sesame or peanut oil or in aqueous propylene glycol may be employed. The aqueous solutions should be suitably buffered (preferably pH greater than 8) if necessary and the liquid diluent first rendered isotonic. These aqueous solutions are suitable for intravenous injection purposes. The oily solutions are suitable for intraarticular, intramuscular and subcutaneous injection purposes. The preparation of all these solutions under sterile conditions is readily accomplished by standard pharmaceutical techniques will known to those skilled in the art.

Additionally, it is also possible to administer the active compounds of the present invention topically and this may be done by way of creams, jellies, gels, pastes, patches, ointments and the like, in accordance with standard pharmaceutical practice.

For administration to animals other than humans, such as cattle or domestic animals, the active compounds may be administered in the feed of the animals or orally as a drench composition.

The active compounds may also be adminstered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine or phosphatidylcholines.

The active compounds may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide phenyl, polyhydroxyethylaspartamide-phenol, or polyethyleneoxide-polylysine substituted with palmitoylresidues. Furthermore, the active compounds may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacrylates and cross-linked or amphipathic block copolymers of hydrogels.

The Examples provided below illustrate specific embodiments of the invention, but the invention is not limited in scope to the Examples specifically exemplified.

Example 1

4"-Acetyl-11-deoxy-11-hydrazo-6-O-methylerythromycin A, 11,12-carbamate

To a solution of 10,11-anhydro-2',4'-di-O-acetyl-12-O-imidazolylcarbonyl-6-O-methylerythromycin A (460 mg, 0.51 mmol) (which was prepared following the procedures of Baker *et al.*, *J. Org. Chem.*, 1988, *53*, 2340), in MeCN at room temperature was added anhydrous NH_2NH_2 (0.16 mL, 5.1 mmol) and the resulting solution was heated at 60°C for 12 hours. MeCN was removed *in vacuo*, brine and EtOAc were added, and the aqueous layer was extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (1.5% Et_3N-1.5% MeOH-97% MeOBu-*t*) to afford the title compound as a white solid (261 mg, 62%) and 4"-acetyl-10-*epi*-11-deoxy-11-hydrazo-6-O-methylerythromycin A, 11,12-carbamate as a white solid (38 mg, 10%).

For the title compound: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.02 (1H, dd, J = 1.6, 10.8 Hz), 4.94 (1H, d, J = 4.8 Hz), 4.65 (1H, d, J = 10.0 Hz), 4.53 (1H, d, J = 7.2 Hz), 4.33 (1H, m), 3.82-3.30 (m), 3.29 (3H, s), 3.20-3.00 (m), 3.00 (3H, s), 2.92-2.31 (m), 2.27 (6H, s), 2.08 (3H, s), 2.0-1.4 (m), and 0.82 (3H, t, J = 7.6 Hz); MS: m/z 830 (M+H).

For 4"-acetyl-10-*epi*-11-deoxy-11-hydrazo-6-O-methylerythromycin A, 11,12-Carbamate: δ: ^{1}H NMR (400 MHz, $CDCl_3$): 5.05 (1H, d, J = 4.4 Hz), 4.87 (1H, dd, J = 1.6, 10.8 Hz), 4.64 (1H, d, J = 10.0 Hz), 4.43 (1H, d, J = 7.6 Hz), 4.33 (1H, m), 3.84-3.32 (m), 3.30 (3H, s), 3.18 (3H, s), 3.2-2.3 (m), 2.23 (6H, s), 2.08 (3H, s), 1.62 (3H, s), 1.30 (3H, s), 0.97 (3H, d, J = 6.8 Hz), and 0.84 (3H, t, J = 7.2 Hz); MS: m/z 830 (M+H).

Example 2

11-Deoxy-5-O-desosaminyl-11-hydrazo-6-O-methylerythronolide A, 11,12-carbamate

A solution of 4"-acetyl-11-deoxy-11-hydrazo-6-O-methylerythromycin A, 11,12-carbamate (40 mg, 0.048 mmol) in EtOH-2N HCl (1 : 2) was stirred at room temperature overnight and the reaction mixture was poured into a cold solution of saturated $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (3 times). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (5% MeOH-0.5% $NH_3 \cdot H_2O$-94.5% CH_2Cl_2) to afford the title compound as a white solid (26.1 mg, 86%):

^1H NMR (400 MHz, $CDCl_3$) δ: 5.09 (1H, dd, J = 2.4, 10.8 Hz), 4.45 (1H, s), 4.38 (1H, d, J = 7.6 Hz), 3.9-3.0 (m), 2.95 (3H, s), 2.75-2.45 (m), 2.27 (6H, s), 2.0-1.4 (m), 1.40 (3H, s), 1.34 (3H, s), 1.24 (3H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.12 (3H, d, J = 7.2 Hz), 1.09 (3H, d, J = 7.2 Hz), 1.07 (3H, d, J = 6.8 Hz), and 0.80 (3H, t, J = 7.6 Hz).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ: 216.90, 175.69, 156.45, 106.65, 88.29, 81.46, 78.74, 78.36, 75.78, 70.63, 70.23, 65.71, 63.37, 49.30, 45.35, 44.66, 40.27 (2C), 39.57, 38.87, 36.07, 28.28, 22.01, 21.23, 18.88, 18.16, 15.19, 14.15, 13.74, 10.14, 8.22.

MS: m/z 629 (M+H).

Example 3

11-Deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methylerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-11-hydrazo-6-O-methyl-erythronolide A, 11,12-carbamate (1.35 g, 21.7 mmol) in anhydrous EtOH (20 mL) was added 3-(4-quinolinyl)propionaldehyde (0.57 g, 3.08 mmol) and the resulting solution was heated at 86°C for two days. EtOH was evaporated *in vacuo* to give the title compound as a white solid (1.84 g, 97%).

^1H NMR (400 MHz, $CDCl_3$) δ: 8.81 (1H, d, J = 4.4 Hz), 8.09 (1H, d, J = 5.2 Hz), 8.07 (1H, d, J = 5.2 Hz), 7.69 (1H, t, J = 8.4 Hz), 7.56 (1H, t, J = 7.2 Hz), 7.29 (1H, d, J = 4.0 Hz), 5.08 (1H, dd, J = 2.0, 10.8Hz), 4.53 (1H, s), 4.41 (1H, d, J = 7.6 Hz), 4.2-3.2 (m), 2.99 (3H, s), 2.9-2.4 (m), 2.25 (6H, s), 2.0-1.5 (m), 1.48 (3H, s), 1.29 (3H, s), 1.30 (3H, d, J = 6.4 Hz), 1.24 (3H, d, J = 6.0 Hz), 1.15 (3H, d, J = 6.4 Hz), 1.10 (3H, d, J = 7.2 Hz), 1.07 (3H, d, J = 6.4 Hz), and 0.87 (3H, t, J = 7.2 Hz).

MS: m/z 794 (M+H).

Example 4

2'-Acetyl-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methylerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methylerythronolide A, 11,12-carbamate (2.07 g, 2.60 mmol) in CH_2Cl_2 (10 mL) was added acetic anhydride (0.49 mL, 5.20 mmol) and the resulting solution was stirred at room temperature for 5 hours. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to give the title compound as a white solid (1.79 g, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.80 (1H, d, J = 4.4 Hz), 8.08 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 9.2 Hz), 8.01 (1H, t, J = 4.8 Hz), 7.68 (1H, dt, J = 1.2, 6.8 Hz), 7.55 (1H, dt, J = 1.2, 6.8 Hz), 7.27 (1H, d, J = 4.4 Hz), 5.02 (1H, dd, J = 2.8, 10 Hz), 4.718 (1H, t, J = 6.7 Hz), 4.40 (1H, s), 4.35 (1H, d, J = 7.6 Hz), 4.19 (1H, d, J = 8.0 Hz), 3.81 (1H, q, J = 6.8 Hz), 3.6-2.4 (m), 2.71 (3H, s), 2.24 (6H, s), 1.9-1.5 (m), 1.55 (3H, s), 1.35 (3H, d, J = 6.8 Hz), 1.33 (3H s), 1.22 (3H, d, J = 6.0 Hz), 1.14 (3H, d, J = 7.6 Hz), 1.10 (3H, d, J = 6.8 Hz), 1.06 (3H, d, J = 6.4 Hz), and 0.87 (3H, t, J = 7.2 Hz).

MS: m/z 837 (M+H).

Example 5

2'-Acetyl-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 2'-acetyl-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methylerythronolide A, 11,12-carbamate (1.69 g, 2.02 mmol) in CH_2Cl_2 (16 mL) was added DMSO (1.85 mL, 8.06 mmol, 10 eq), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDAC) (1.55 g, 8.06 mmol, 3.1 eq), and Py•TFA (1.56 g, 8.06 mmol, 3.1 eq) and the resulting suspension was stirred at room temperature for 2 hours. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (5% MeOH-0.5% NH_3•H_2O-94.5% CH_2Cl_2) to afford the title compound as a white solid (1.59 g, 94%).

^{1}H NMR (400 MHz, $CDCl_3$): 8.79 (1H, d, J = 3.6 Hz), 8.08 (1H, d, J = 8.8 Hz), 8.05 (1H, d, J = 8.4 Hz), 8.00 (1H, t, J = 4.8 Hz), 7.69 (1H, t, J = 8.4 Hz), 7.55 (1H, t, J = 7.2 Hz), 7.27 (1H, d, J = 4.4 Hz), 5.03 (1H, dd, J = 2.4, 10.0 Hz), 4.70 (1H, dd, J = 7.6, 10.4 Hz), 4.39 (1H, s), 4.34 (1H, d, J = 7.6 Hz), 4.18 (1H, d, J = 8.0 Hz), 3.82 (1H, q, J = 6.8 Hz), 3.6-1.6 (m), 2.71 (3H, s), 2.22 (6H, s), 2.03 (3H, s), 1.54 (3H, s), 1.33 (3H, d, J = 6.4 Hz), 1.28 (3H, s), 1.21 (3H, d, J = 6.4 Hz), 1.14 (3H, d, J = 7.6 Hz), 1.09 (3H, d, J = 6.8 Hz), 1.06 (3H, d, J = 6.8 Hz), 0.87 (3H, t, J = 7.2 Hz).

MS: m/z 836 (M+H).

Example 6

11-Deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl))hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

To a solution of 2'-acetyl-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (1.59 g, 1.90 mmol) in MeOH (25 mL) at room temperature was added $NaBH_3CN$ (359 mg, 5.70 mmol, 3 eq) followed by HOAc (0.65 mL, 11.4 mmol, 6 eq) and the resulting reaction mixture was stirred at room temperature overnight. MeOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in MeOH (50 mL) and the solution was heated under reflux for 1 hour. MeOH was then removed *in vacuo* and the crude product was purified by silica gel flash chromatography (5% MeOH-0.5% $NH_3 \cdot H_2O$-94.5% CH_2Cl_2) to afford the title compound as a white solid (1.13 g, 75%).

^1H NMR (400 MHz, $CDCl_3$) δ: 8.75 (1H, d, J = 4.27 Hz), 8.07 (2H, t, J = 9.4 Hz), 7.64 (1H. dt, J = 1.6, 6.8 Hz), 7.50 (1H, dt, J = 1.6, 7.2 Hz), 7.26 (1H, d, J = 4.4 Hz), 5.47 (1H, t, J = 3.6 Hz), 4.98 (1H, d, J = 10.8 Hz), 4.26 (1H, s), 4.24 (1H, s), 3.84 (1H, q, J = 6.8 Hz), 3.71 (1H, s), 3.8-2.7 (m), 2.62 (3H, s), 2.6-2.3 (m), 2.22 (6H, s), 2.2-1.5 (m), 1.44 (3H, s), 1.33 (3H, d, J = 6.8 Hz), 1.31 (3H, s), 1.29 (3H, d , J = 7.6 Hz), 1.21 (3H, d, J = 6.0 Hz), 1.16 (3H, d, J 6.0 Hz), 1.04 (3H, d, J = 6.8 Hz), and 0.78 (3H, t, J = 7.2 Hz).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ (attached H's): 217.82 (0), 203.63 (0), 169.72 (0), 156.10 (0), 150.18 (1), 148.20 (2C, 0), 130.05 (1), 128.85 (1), 127.58 (0), 126.19 (1), 123.81 (1), 120.97 (1), 103.96 (1), 80.69 (0), 79.37 (1), 78.12 (0), 77.35 (1), 70.33 (1), 69.63 (1), 65.84 (1), 58.14 (1), 51.04 (1), 50.13 (3), 48.41 (2), 47.31 (1), 44.55 (1), 40.19 (2C, 3), 39.60 (2C, 2 and 1), 29.49 (2), 28.47 (2), 28.14 (2), 22.03 (2), 21.14 (3), 19.82 (3), 18.50 (3), 15.31 (3), 14.55 (3), 14.38 (3), 14.21 (3), and 10.35 (3).

MS: m/z 797 (M+H).

Example 7

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl))hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

Method I:

To a solution of 11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (654 mg, 0.82 mmol) in *i*-PrOH (8.0 mL) was added $NH_2OH \cdot HCl$ (855 mg, 12.3 mmol, 15 eq) and the reaction mixture was heated at 90°C for six days. *i*-PrOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in*

vacuo. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid (224 mg, 34%) and the recovered starting material (107 mg, 16%).

^1H NMR (400 MHz, $CDCl_3$) δ: 10.85 (1H, br s), 8.39 (1H, d, J = 4.4 Hz), 8.00 (1H, d, J = 8.4 Hz), 7.90 (1H, d, J = 8.0 Hz), 7.60 (1H, t, J = 7.2 Hz), 7.42 (1H, t, J = 7.6 Hz), 6.82 (1H, d, J = 4.8 Hz), 5.05 (1H, dd, J = 2.0, 10.8 Hz), 4.30 (1H, dd, J = 5.6, 7.2 Hz), 3.89 (1H, q, J = 6.4 Hz), 3.92 (1H, s), 3.55 (1H, m), 3.27 (1H, m), 3.15-2.50 (m), 2.83 (3H, s), 2.35 (6H, s), 1.95 (1H, m), 1.8-1.2 (m), 1.55 (3H, s), 1.49 (3H, s), 1.35 (3H, d, J = 6.8 Hz), 1.29 (3H, d, J = 7.6 Hz), 1.26 (3H, d, J = 6.0 Hz), 1.15 (3H, d, J = 6.8 Hz), 1.03 (3H, d, J = 6.8 Hz), and 0.825 (3H, t, J = 7.2 Hz).

^{13}C NMR (100.6 MHz, $CDCl_3$) δ (attached H's): 203.73 (0), 169.85 (0), 166.52 (0), 156.35 (0), 149.22 (1), 147.06 (0), 129.35 (1), 128.85 (1), 127.36 (0), 126.41 (1), 123.77 (1), 120.24 (1), 103.91 (1), 81.28 (0), 79.77 (1), 78.66 (0), 77.37 (1), 70.34 (1), 69.40 (1), 65.95 (1), 59.68 (1), 51.16 (1), 50.52 (3), 48.08 (2), 47.52 (1), 40.26 (2C, 3), 38.26 (2), 33.66 (1), 29.40 (2), 28.51 (2), 27.93 (2), 25.59 (1), 22.17 (2), 21.18 (3), 20.09 (3), 19.15 (3), 17.40 (3), 15.37 (3), 14.52 (3), 14.36 (3), and 10.44 (3).

MS: m/z 812 (M+H).

Method II:

To a solution of 9-deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (186 mg, 0.23 mmol), prepared according to the procedures as described in Example 17, in methanol was added HOAc (212 uL, 3.7 mmol) and $NaBH_3CN$ (158 mg, 2.3 mmol) and the resulting mixture was stirred at room temperature for 12 h. MeOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (5% MeOH-0.5% $NH_3 \cdot H_2O$-94.5% CH_2Cl_2) to afford the title compound as a white solid (114 mg, 61%).

Example 8

<u>9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl))hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate</u>

Method I: To a solution of 11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (50 mg, 0.063 mmol) in *i*-PrOH (1.0 mL) was added $NH_2OMe \cdot HCl$ (26 mg, 0.31 mmol, 5 eq) and the reaction mixture was heated at 90°C for three days. *i*-PrOH was removed *in vacuo* and the residue was

dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid (27 mg, 52%) and some recovered starting material.

^1H NMR (400 MHz, $CDCl_3$) δ: 8.75 (1H, d, J = 4.4 Hz), 8.12 (1H, d, J = 8.4 Hz), 8.06 (1H, d, J = 8.8 Hz), 7.65 (1H, t, J = 6.8 Hz), 7.50 (1H, t, J = 6.8 Hz), 7.27 (1H, d, J = 4.4 Hz), 6.04 (1H, br s), 5.01 (1H, d, J = 9.6 Hz), 4.3-1.4 (m), 3.86 (1H, q, J = 6.8 Hz), 3.70 (3H, s), 2.66 (3H, s), 2.31 (6H, s), 1.45 (3H, s), 1.37 (3H, s), 1.33 (3H, d, J = 6.8 Hz), 1.27 (3H, d, J = 7.2 Hz), 1.24 (3H, d, J = 6.0 Hz), 1.10 (3H, d, J = 6.4Hz), 0.98 (3H, d, J = 6.8 Hz), and 0.77 (3H, t, J = 7.6 Hz).

MS: m/z 826 (M+H).

Method II: The title compound was prepared from 9-deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate and 3-quinolin-4-yl-propioaldehyde following the procedures as described in Example 11.

Example 9

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl))hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (40 mg, 0.050 mmol) in *i*-PrOH (1.0 mL) was added $NH_2OBn \cdot HCl$ (32 mg, 0.20 mmol) and the reaction mixture was heated at 90°C for three days. *i*-PrOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid (10 mg, 22%) and some recovered starting material.

^1H NMR (400 MHz, $CDCl_3$): 8.75 (1H, d, J = 4.4 Hz), 8.10 (1H, d, J = 8.4 Hz), 8.07 (1H, d, J = 8.4 Hz), 7.65 (1H, t, J = 7.2 Hz), 7.49 (1H, t, J = 8.4 Hz), 7.30 (6H, m), 5.82 (1H, br s), 4.99 (1H, d, J = 8.0 Hz), 4.95 (1H, d, J = 12.4 Hz, AB), 4.85 (1H, d, J = 12.4 Hz, AB), 4.3-1.4 (m), 3.86 (1H, q, J = 6.8 Hz), 2.67 (3H, s), 2.30 (6H, s), 1.44 (3H, s), 1.40 (3H, s), 1.33 (3H, d, J = 6.8 Hz), 1.28 (3H, d, J = 7.6 Hz), 1.25 (3H, d, J = 6.0 Hz), 1.07 (3H, d, J = 7.2 Hz), 0.95 (3H, d, J = 6.8 Hz), and 0.75 (3H, t, J = 7.2 Hz).

MS: m/z 902 (M+H).

Example 10

9-Deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-11-hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (600 mg, 0.96 mmol) in EtOH (9.0 mL) was added $NH_2OMe{\cdot}HCl$ (319 mg, 3.83 mmol, 4.0 eq) and the reaction mixture was heated at 80°C for 48 hours. EtOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give the title compound as a white solid (602 mg).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.77 (3H, s), 2.68 (3H, s), 2.25 (6H, s), 1.43 (s, 3H), 1.38 (3H, s), 1.33 (3H, d, J = 7.2 Hz), 1.27 (3H, d, J = 7.6 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.13 (3H, d, J = 6.8 Hz), 0.98 (3H, d, J = 6.8 Hz), and 0.83 (3H, t, J = 7.6 Hz).

MS: m/z 657 (M+H).

Example 11

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-pyridin-3-yl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 9-Deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (300 mg, 0.45 mmol) in toluene (4.0 mL) was added 3-(4-pyridin-3-yl-imidazol-1-yl)-propioaldehyde (100 mg, 0.50 mmol, 1.1 eq) and the reaction mixture was heated at 90°C for 18 hours. Toluene was removed *in vacuo* and the residue was dissolved in MeOH (4.0 mL). HOAc (0.39 mL, 6.8 mmol) and $NaBH_3CN$ (427 mg, 6.8 mmol) were added and the resulting solution was stirred at room temperature for 14 hours. MeOH was evaporated in vacuo, saturated $NaHCO_3$ was added to the residue, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3{\cdot}H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid.

^1H NMR (400 MHz, $CDCl_3$) δ: 8.94 (1H, s), 8.42 (1H), 8.03 (1H), 7.58 (1H, s), 7.36 (1H, s), 7.25 (1H), 6.11 (1H, s), 3.69 (3H, s), 2.64 (3H, s), 2.23 (6H, s), 1.45 (3H, s), 1.36 (3H, s), 1.30 (3H, d, J = 5.6 Hz), 1.26 (3H, d, J = 6.8 Hz), 1.21 (3H, d, J = 4.8 Hz), 1.09 (3H, d, J = 6.8 Hz), 0.97 (3H, d, J = 6.4 Hz), and 0.80 (3H, t, J = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.41, 170.01, 167.63, 156.73, 147.56, 146.40, 138.94, 138.13, 131.85, 130.31, 123.47, 115.12, 103.99, 81.36, 79.51, 78.51, 77.27, 70.33, 69.58, 65.84, 61.30, 59.24, 51.06, 50.40, 47.37, 44.39, 44.35, 40.23 (2C), 38.21, 33.86, 29.28, 28.12, 26.48, 22.11, 21.18, 19.91, 18.97, 17.45, 15.19, 14.49, 14.33, and 10.53.

MS: m/z 842 (M+H).

Example 12

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(imidazo(4,5-b)pyridin-3-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 9-Deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (2.0 g, 3.05 mmol) in toluene (30 mL) was added 3-(imidazo(4,5-b)pyridin-3-yl)-propioaldehyde (910 mg, 4.26 mmol, 1.4 eq) and the reaction mixture was heated at 90°C for 18 hours. Toluene was removed *in vacuo* and the residue was dissolved in MeOH (30 mL). HOAc (2.8 mL, 48.72 mmol) and $NaBH_3CN$ (1.91 g, 30.45 mmol) were added and the resulting solution was stirred at room temperature for 14 hours. MeOH was evaporated in vacuo, saturated $NaHCO_3$ was added to the residue, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid.

^1H NMR (400 MHz, $CDCl_3$) δ: 8.35 (1H), 8.22 (1H, s), 8.02 (1H), 7.20 (1H), 7.36 (1H, s), 6.10 (1H, br t), 3.47 (3H, s), 2.62 (3H, s), 2.24 (6H, s), 1.46 (3H, s), 1.37 (3H, s), 1.30 (3H, d, J = 6.8 Hz), 1.27 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.0 Hz), 1.12 (3H, d, J = 6.8 Hz), 0.99 (3H, d, J = 7.2 Hz), and 0.84 (3H, t, J = 7.6 Hz).

MS: m/z 816 (M+H).

Example 13

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 9-Deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (1.37 g, 2.09 mmol) in toluene (14 mL) was added 3-(4-phenyl-imidazol-1-yl)-propioaldehyde (583 mg, 2.92 mmol, 1.4 eq) and the reaction mixture was heated at 90°C for 18 hours. Toluene was removed *in vacuo* and the residue was dissolved in MeOH (20 mL). HOAc (1.8 mL, 31.35 mmol) and $NaBH_3CN$ (1.97 g, 31.35 mmol) were added and the resulting solution was stirred at room temperature for 14 hours. MeOH was evaporated in vacuo, saturated $NaHCO_3$ was added to the residue, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid.

^1H NMR (400 MHz, $CDCl_3$) δ: 8.35 (1H), 8.22 (1H, s), 8.02 (1H), 7.20 (1H), 7.36 (1H, s), 6.10 (1H, br t), 3.69 (3H, s), 2.66 (3H, s), 2.26 (6H, s), 1.46 (3H, s), 1.37 (3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.27 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.0 Hz), 1.11 (3H, d, J = 7.2 Hz), 0.98 (3H, d, J = 7.2 Hz), and 0.83 (3H, t, J = 7.2 Hz).

MS: m/z 841 (M+H).

Example 14

9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (202 mg, 0.322 mmol) in MeOH (3.0 mL) was added $NH_2OBn \cdot HCl$ (225 mg, 1.41 mmol, 4.4 eq) and the reaction mixture was heated at 72°C for 16 hours. MeOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid.

^1H NMR (400 MHz, $CDCl_3$) δ: 7.25 (5H, m), 5.39 (4H, br s), 5.09 (1H, d, J = 12.8 Hz, AB), 4.99 (1H, d, J = 12.8 Hz, AB), 4.93 (1H, dd, J = 3.2, 9.2 Hz), 4.30 (1H, d, J = 7.2 Hz), 3.98 (1H, d, J = 10.8 Hz), 3.54 (1H, q, J = 6.8 Hz), 3.9-1.3 (m), 2.75 (3H, s), 2.27 (6H, s), 2.02 (3H, d, J = 6.8 Hz), 1.30 (3H, s), 1.27 (3H, d, J = 7.2 Hz), 1.22 (3H, s), 1.21 (3H, d, J = 6.8 Hz), 1.20 (3H, d, J = 6.8 Hz), 1.09 (3H, d, J = 7.2 Hz), and 0.814 (3H, t, J = 7.6 Hz).

MS: m/z 733 (M+H).

Example 15

9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (499 mg, 0.795 mmol) in *i*-PrOH (7.0 mL) was added NH_2OH•HCl (579 mg, 8.33 mmol, 10.5 eq) and the reaction mixture was heated at 80°C for three days. *i*-PrOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% NH_3•H_2O-89% CH_2Cl_2) to afford a 3 : 2 mixture of the title compound as a white solid (157 mg, 31%).

^1H NMR (400 MHz, $CDCl_3$) of the major isomer, δ: 2.77 (3H, s, 6-OMe), 2.26 (6H, s, NMe_2), 0.84 (3H, t,, J = 7.0 Hz, 15-Me); MS: m/z 610 (M+H).

^1H NMR (400 MHz, $CDCl_3$) of the minor isomer, δ: 2.68 (3H, s, 6-OMe), 2.25 (6H, s, NMe_2), 0.81 (3H, t,, J = 7.0 Hz, 15-Me); MS: m/z 610 (M+H).

Example 16

9-Deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 11-deoxy-5-O-desosaminyl-11-hydrazo-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (20 g, 31.8 mmol) in EtOH (210 mL) was added NH_2OH•HCl (33.1g, 477 mmol, 15 eq) and pyridine (38.4 mL, 477 mmol, 15 eq), and the resulting solution at 80°C for 38 h. EtOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by silica gel flash chromatography (3% MeOH-0.3% NH_3•H_2O-96.7% CH_2Cl_2) to afford the title compound as a white solid (7.3g).

^1H NMR (400 MHz, $CDCl_3$) δ: 9.81 (1H, br. s), 2.67 (3H, s), 2.57 (1H, q, J = 6.8 Hz), 2.25 (6H, s), 1.47 (3H, s), 1.43 (3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.21 (3H, d, J = 6.4 Hz), 1.11 (3H, d, J = 6.8 Hz), 0.97 (3H, d, J = 7.2 Hz), 0.83 (3H, t, J = 7.2Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.81, 169.80, 165.97, 156.68, 103.91, 81.53, 79.85, 78.49, 76.74, 70.35, 69.48, 65.85, 64.33, 51.10, 49.66, 47.73, 40.24, 38.42, 33.73, 28.19, 25.55, 22.11, 21.15, 19.98, 18.64, 16.96, 15.68, 14.25, 13.71, and 10.39.

MS: m/z 643 (M+H).

Example 17

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 9-deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (150 mg, 0.23 mmol) in anhydrous toluene (2.3 mL) was added 3-(4-quinolinyl)propionaldehyde (85 mg, 0.46 mmol) and the resulting solution was heated at 90°C for 18 h. EtOH was evaporated *in vacuo* and the crude product was purified by silica gel flash chromatography (5% MeOH-0.5% $NH_3 \cdot H_2O$-94.5% CH_2Cl_2) to afford the title compound.

^1H NMR (400 MHz, $CDCl_3$) δ: 2.84 (3H, s), 2.30 (6H, s), 1.58 (3H, s), 1.54 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.32 (3H, d, J = 7.2 Hz), 1.28 (3H, d, J = 6.0 Hz), 1.25 (3H, d, J = 6.0 Hz), 1.05 (3H, d, J = 7.2 Hz), 0.86 (3H, t, J = 7.2 Hz).

MS: m/z 810 (M+H).

Example 18

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzoimidazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

To a solution of 9-deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate (100 mg, 0.16 mmol) in anhydrous toluene (1.6 mL) was added 3-(benzoimidazol-1-yl)propionaldehyde (62 mg, 0.36 mmol) and the resulting solution was heated at 90°C for 18 h. EtOH was evaporated *in vacuo* and the crude product was dissolved in methanol (1.5 mL). To this solution was added HOAc (137uL, 2.4 mmol) and $NaBH_3CN$ (103 mg, 1.5 mmol) and the resulting mixture was stirred at room temperature for 12 h. MeOH was removed *in vacuo* and the residue was dissolved in CH_2Cl_2. Saturated $NaHCO_3$ was added, the aqueous layer was extracted with CH_2Cl_2 (3 times), the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (10% MeOH-1% $NH_3 \cdot H_2O$-89% CH_2Cl_2) to afford the title compound as a white solid (57 mg, 46%).

^1H NMR (400 MHz, $CDCl_3$) δ: 11. 00 (1H, br s), 2.71 (3H, s), 2.30 (6H, s), 1.49 (3H, s), 1.47 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.28 (3H, d, J = 7.6 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.11 (3H, d, J = 7.2 Hz), 0.99 (3H, d, J = 6.8 Hz), and 0.824 (3H, t, J = 7.2 Hz).
2.84 (3H, s), 2.30 (6H, s), 1.58 (3H, s), 1.54 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.32 (3H, d, J = 7.2 Hz), 1.28 (3H, d, J = 6.0 Hz), 1.25 (3H, d, J = 6.0 Hz), 1.05 (3H, d, J = 7.2 Hz), 0.86 (3H, t, J = 7.2 Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.45, 169.92, 166.21, 156.74, 143.31, 142.85, 133.53, 122.90, 122.12, 119.47, 110.23, 103.93, 81.33, 79.87, 78.59, 77.24, 70.29, 69.38, 65.97, 59.68,

51.09, 50.62, 47.45, 44.45, 42.34, 40.26, 38.23, 33.59, 28.49, 27.40, 25.55, 22.18, 21.15, 20.10, 19.11, 17.32, 15.28, 14.53, 14.39, and 10.51.

MS: m/z 801 (M+H).

The following compounds were prepared from 9-deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate and appropriate aldehydes by using the procedures as described above.

Example 19

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.69 (3H, s), 2.29 (6H, s), 1.49 (3H, s), 1.47 (3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.27 (3H, d, J = 7.6 Hz), 1.24 (3H, d, J = 6.0 Hz), 1.10 (3H, d, J = 6.8 Hz), 1.00 (3H, d, J = 6.8 Hz), and 0.83 (3H, t, J = 7.2 Hz).

MS: m/z 801 (M+H).

Example 20

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.95 (1H, br. s), 1.44 (3H, s), 1.39 (3H, s), 1.25 (6H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.09 (3H, d, J = 6.8 Hz), 1.03 (3H, d, J = 6.8 Hz), and 0.81 (3H, t, J = 7.6 Hz).

MS: m/z 802 (M+H).

Example 21

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.02 (1H, br. s), 6.23 (1H, br. s), 2.58 (3H, s), 2.32 (6H, s), 1.47 (6H, s), 1.29 (3H, d, J = 6.8 Hz), 1.26 (3H, d, J = 7.6 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.10 (3H, d, J = 6.8 Hz), 1.01 (3H, d, J = 6.8 Hz), and 0.81 (3H, t, J = 7.2 Hz).

MS: m/z 802 (M+H).

Example 22

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-phenylpropyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.59 (1H, br. s), 7.10 (5H, m), 6.55 (1H, br. s), 2.67 (3H, s), 2.24 (6H, s), 1.43 (6H, s), 1.33 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.2 Hz), 1.21 (3H, d, J = 6.0 Hz), 1.00 (3H, d, J = 6.8 Hz), 0.92 (3H, d, J = 6.4 Hz), and 0.82 (3H, t, J = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.70, 169.59, 166.73, 156.24, 142.12, 128.42 (2C), 128.20 (2C), 125.62, 103.94, 81.35, 79.63, 78.56, 77.11, 70.36, 69.48, 65.87, 59.50, 51.13, 50.40, 48.02, 47.52, 40.24 (2C), 38.21, 33.60, 33.14, 29.77, 28.21, 25.57, 22.19, 21.15, 20.13, 19.05, 17.13, 15.41, 14.46, 14.29, and 10.49.

MS: m/z 761 (M+H).

Example 23

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-hydroxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.91 (2H), 6.68 (2H), 6.43 (1H, br. s), 2.67 (3H, s), 2.30 (6H, s), 1.44 (3H, s), 1.43 (3H, s), 1.33 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.2 Hz), 1.21 (3H, d, J = 6.0 Hz), 1.01 (3H, d, J = 6.8 Hz), 0.92 (3H, d, J = 6.4 Hz), and 0.80 (3H, t, J = 7.2 Hz).

MS: m/z 778 (M+H).

Example 24

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.38 (1H, br. s), 7.04 (2H, d, J = 8.4 Hz), 6.74 (2H, d, J = 8.4 Hz), 6.44 (1H, br. s), 3.74 (3H, s), 2.67 (3H, s), 2.30 (6H, s), 1.44 (6H, s), 1.33 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.0 Hz), 1.01 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 6.8 Hz), and 0.82 (3H, t, J = 7.2 Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.71, 169.58, 167.06, 157.64, 156.30, 134.23, 129.29 (2C), 113.68 (2C), 103.84, 81.33, 79.61, 78.51, 77.16, 70.27, 69.34, 65.98, 59.51, 55.19, 51.12, 50.44, 47.95, 47.45, 40.26 (2C), 38.19, 33.64, 32.29, 30.06, 28.46, 25.55, 22.19, 21.12, 20.09, 19.05, 17.17, 15.34, 14.49, 14.33, and 10.49.

MS: m/z 792 (M+H).

Example 25

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.66 (1H, br. s), 7.13 (2H), 6.82 (2H), 3.80 (3H, s), 2.68 (3H, s), 2.30 (6H, s), 1.45 (3H, s), 1.43 (3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.26 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.4 Hz), 1.06 (3H, d, J = 6.8 Hz), 0.98 (3H, d, J = 6.4 Hz), and 0.83 (3H, t, J = 7.2 Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.78, 169.59, 167.39, 157.04, 156.14, 130.36, 129.29, 126.96, 120.82, 110.49, 103.86, 81.19, 79.16, 78.42, 77.24, 70.27, 69.37, 65.94, 59.88, 55.54, 51.10, 50.56, 48.26, 47.34, 40.24 (2C), 38.22, 33.70, 28.44, 27.83, 27.45, 25.58, 22.19, 21.13, 20.01, 19.07, 17.29, 15.21, 14.50, 14.43, and 10.37.

MS: m/z 792 (M+H).

Example 26

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(benzyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (1H, br. s), 6.23 (1H, br. s), 2.88 (3H, s), 2.29 (6H, s), 1.51 (3H, s), 1.44 (3H, s), 1.36 (3H, d, J = 6.8 Hz), 1.29 (3H, d, J = 7.6 Hz), 1.25 (3H, d, J = 6.0 Hz), 1.05 (3H, d, J = 6.8 Hz), 0.97 (3H, d, J = 7.2 Hz), and 0.75 (3H, t, J = 7.6 Hz).

MS: m/z 733 (M+H).

Example 27

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(pyridin-4-yl-methyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (2H), 7.25 (2H), 6.39 (1H, br. s), 2.87 (3H, s), 2.27 (6H, s), 1.54 (3H, s), 1.46 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.29 (3H, d, J = 7.2 Hz), 1.24 (3H, d, J = 6.0 Hz), 1.13 (3H, d, J = 6.8 Hz), 1.01 (3H, d, J = 7.2 Hz), 0.76 (3H, t, J = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.72, 169.91, 166.50, 155.76, 148.16 (2C), 147.70, 123.71 (2C), 103.99, 81.17, 79.75, 78.71, 77.26, 70.34, 69.50, 65.92, 60.30, 51.69, 51.15, 50.74, 47.62, 40.26 (2C), 38.25, 33.69, 28.29, 25.54, 22.02, 21.16, 20.16, 19.14, 17.36, 15.42, 14.50, 14.29, and 10.27.

MS: m/z 733 (M+H).

Example 28

9-Deoxo-11-deoxy-5-O-desosaminyl-11-3-(pyridin-4-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 11.62 (1H, s), 8.24 (2H), 6.91 (2H), 6.20 (1H, br. s), 2.76 (3H, s), 2.31 (6H, s), 1.51 (3H, s), 1.46 (3H, s), 1.33 (3H, d, J = 6.4 Hz), 1.27 (3H, d, J = 7.2 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.10 (3H, d, J = 6.8 Hz), 1.00 (3H, d, J = 6.8 Hz), 0.83 (3H, t, J = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ:203.71, 169.78, 166.30, 156.35, 152.39, 140.45, 124.10 (2C), 124.10 (2C), 103.86, 3, 79.71, 78.59, 77.24, 70.27, 69.34, 65.98, 59.50, 51.15, 50.44, 47.55 (2C), 40.27 (2C), 38.21, 33.60, 32.50, 28.54, 27.90, 25.51, 22.14, 21.13, 20.11, 19.11, 17.33, 15.42, 14.48, 14.32, and 10.44.

MS: m/z 762(M+H).

Example 29

9-Deoxo-11-deoxy-5-O-desosaminyl-11-3-(pyridin-3-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.96 (1H, s), 8.30 (1H, d, J = 4.4 Hz), 8.21 (1H, s), 7.40 (1H, d, J = 8.0 Hz), 7.10 (1H, dd, J = 5.2 and 7.6 Hz), 6.16 (1H, br. s), 2.70 (3H, s), 2.27 (6H, s), 1.48 (3H, s), 1.44 (3H, s), 1.31 (3H, d, J = 7.2 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.21 (3H, d, J = 6.0 Hz), 1.06 (3H, d, J = 6.8 Hz), 0.96 (3H, d, J = 6.8 Hz), 0.80 (3H, t, J = 7.6 Hz).

MS: m/z 762(M+H).

Example 30

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(phenylethyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ:7.25 (5H, m), 2.59 (3H, s), 2.28 (6H, s), 1.40 (3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.30 (3H, s), 1.25 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.0 Hz), 0.98 (3H, d, J = 6.8 Hz), 0.88 (3H, d, J = 6.8 Hz), 0.83 (3H, t, J = 7.6 Hz).

MS: m/z 747 (M+H).

Example 31

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.65 (1H, br. s), 7.87 (2H, d, J = 8.4 Hz), 6.92 (2H, d, J = 9.2 Hz), 6.16 (1H, br. s), 3.80 (3H, s), 2.46 (3H, s), 2.24 (6H, s), 1.03 (3H, d, J = 7.2 Hz), 0.96 (3H, d, J = 7.2 Hz), and 0.81 (3H, t, J = 7.2 Hz).

MS: m/z 859 (M+H).

Example 32

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-chlorophenyl)-(1,2,4)oxadizol-5-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (2H, d, J = 8.8 Hz), 7.39 (2H, d, J = 8.8 Hz), 6.20 (1H, br. s), 2.49 (3H, s), 2.24 (6H, s), 1.42 (3H, s), 1.03 (3H, d, J = 7.2 Hz), 0.96 (3H, d, J = 6.8 Hz), and 0.82 (3H, t, J = 7.2 Hz).

MS: m/z 863 (M+H).

Example 33

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (1H, br. s), 8.02 (1H), 7.28 (1H), 7.12 (1H), 7.04 (1H), 6.89 (1H), 6.23 (1H, br. s), 2.60 (3H, s), 2.30 (6H, s), 1.44 (3H, s), 1.39 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.22 (3H, d, J = 6.4 Hz), 1.02 (3H, d, J = 7.2 Hz), 0.92 (3H, d, J = 6.8 Hz), and 0.82 (3H, t, J = 7.6 Hz).

MS: m/z 800 (M+H).

Example 34

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.53 (1H, br. s), 7.91 (1H), 7.68 (1H), 7.44 (1H), 7.26 (1H), 7.12 (1H), 6.40 (1H, br. s), 2.54 (3H, s), 2.25 (6H, s), 1.48 (3H, s), 1.44 (3H, s), 1.08 (3H, d, J = 6.8 Hz), 1.02 (3H, d, J = 7.2 Hz), and 0.79 (3H, t, J = 7.2 Hz).

MS: m/z 801 (M+H).

Example 35

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(5-phenyl-1H-pyrrol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.36 (1H, br. s), 7.49 (2H), 7.30 (2H), 7.10 (1H), 6.35 (1H), 5.88 (1H), 2.66 (3H, s), 2.25 (6H, s), 1.45 (3H, s), 1.38(3H, s), 1.32 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.18 (3H, d, J = 6.4 Hz), 1.05 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 7.2 Hz), and 0.72 (3H, t, J = 7.2 Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.54, 169.84, 167.07, 156.85, 133.90, 133.21, 130.84, 128.58, 125.11, 123.35, 106.83, 105.41, 103.89, 81.18, 79.60, 78.52, 77.17, 70.27, 69.37, 65.90, 59.84, 51.12, 50.52, 47.76, 47.49, 40.23, 38.17, 33.64, 28.56, 28.36, 25.57, 25.01, 22.22, 21.12, 20.00, 19.04, 17.19, 15.37, 14.48, 14.28, and 10.39.

MS: m/z 826 (M+H).

Example 36

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-carbazol-9-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (2H), 7.46 (2H), 7.38 (2H), 7.12 (2H), 2.55 (3H, s), 2.23 (6H, s), 1.44 (3H, s), 1.40(3H, s), 1.35 (3H, d, J = 7.2 Hz), 1.03 (3H, d, J = 6.8 Hz), 0.94 (3H, d, J = 6.8 Hz), and 0.76 (3H, t, J = 7.2 Hz).

MS: m/z 851 (M+H).

Example 37

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(1H-indol-3-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (1H, br. s), 7.98 (1H), 7.55 (1H), 7.25 (1H), 7.12 (1H), 7.05 (1H), 6.86 (1H), 6.21 (1H, br. s), 2.58 (3H, s), 2.26 (6H, s), 1.44 (3H, s), 1.39(3H, s), 1.34 (3H, d, J = 6.0 Hz), 1.01 (3H, d, J = 6.4 Hz), 0.92 (3H, d, J = 6.8 Hz), and 0.81 (3H, t, J = 7.2 Hz).

MS: m/z 800 (M+H).

Example 38

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-furan-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.18 (1H, br. s), 7.21 (1H, s), 5.93 (1H, s), 6.42 (1H, br. s), 5.93 (1H, s), 2.68 (3H, s), 2.25 (6H, s), 1.45 (3H, s), 1.44 (3H, s), 1.32 (3H, d, J = 6.4 Hz), 1.26 (3H, d, J = 7.2 Hz), 1.21 (3H, d, J = 6.4 Hz), 1.01 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 6.8 Hz), and 0.83 (3H, t, J = 7.2 Hz).

^{13}H NMR (100 MHz, $CDCl_3$) δ: 203.71, 169.61, 167.70, 156.30, 155.74, 140.73, 110.02, 104.94, 103.94, 81.34, 79.65, 78.51, 77.11, 70.34, 69.51, 65.86, 59.55, 51.11, 50.44, 47.61, 47.50, 40.25 (2C), 38.20, 33.60, 28.16, 26.22, 25.58, 25.22, 22.19, 21.17, 20.14, 19.07, 17.13, 15.39, 14.47, 14.33, and 10.47.

MS: m/z 751 (M+H).

Example 39

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrrol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.51 (1H, br. s), 7.21 (1H, s), 6.64 (1H), 6.05 (1H), 2.68 (3H, s), 2.33 (6H, s), 1.45 (3H, s), 1.43 (3H, s), 1.32 (3H, d, J = 6.4 Hz), 1.26 (3H, d, J = 7.2 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.01 (3H, d, J = 6.8 Hz), 0.93 (3H, d, J = 7.2 Hz), and 0.84 (3H, t, J = 7.2 Hz).

MS: m/z 750 (M+H).

Example 40

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.83 (1H, br. s), 7.40 (1H), 7.28 (1H), 6.20 (1H), 6.05 (1H), 2.52 (3H, s), 2.24 (6H, s), 1.45 (3H, s), 1.43 (3H, s), 1.28 (3H, d, J = 6.4 Hz), 1.24 (3H, d, J = 7.6 Hz), 1.19 (3H, d, J = 6.4 Hz), 1.05 (3H, d, J = 6.8 Hz), 0.99 (3H, d, J = 6.8 Hz), and 0.80 (3H, t, J = 7.2 Hz).

MS: m/z 751 (M+H).

Example 41

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-naphthalen-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.32 (1H, br. s), 8.04 (1H), 7.76 (1H), 7.61 (1H), 7.40 (2H), 7.24 (2H), 2.65 (3H, s), 2.31 (6H, s), 1.44 (3H, s), 1.42 (3H, s), 1.34 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 7.6 Hz), 1.23 (3H, d, J = 6.0 Hz), 1.02 (3H, d, J = 6.8 Hz), 0.94 (3H, d, J = 6.8 Hz), and 0.79 (3H, t, J = 7.6 Hz).

MS: m/z 811 (M+H).

The following compounds can be prepared from 9-deoxo-11-deoxy-5-O-desosaminyl-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate and appropriate aldehydes by using the procedures as described as above.

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-1H-imidazol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-pyridin-3-yl-thiazol-4-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-phenyl-thiazol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

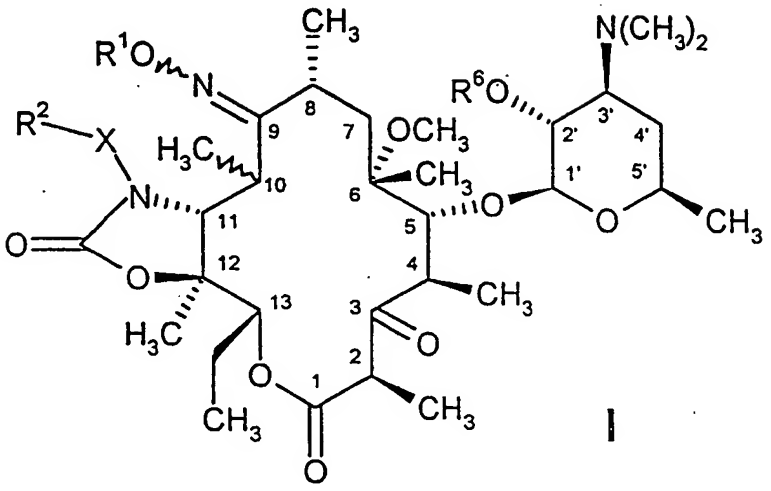
9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-thiophen-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(7-methoxy-quinolin-4-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate.

CLAIMS

What is claimed is:

1. A compound of the formula



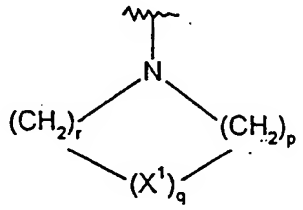
I

or a pharmaceutically acceptable salt thereof, wherein:

X is $-CR^7R^8-$ or $-NR^7-$;

or X is taken together with R^2 to form $-N=CR^4R^5$;

or X and R^2 are taken together to form a heterocyclic ring of the formula XVI:



XVI

wherein in said ring of formula XVI, r and p are each independently an integer ranging from 1 to 3, q is 0 or 1, and X^1 is $-CH_2-$, O, S, -C(O)-, -C(S)-, $-SO_2-$, -CH=CH-, -CH(OH)CH(OH)-, or -NH-; and wherein the $(CH_2)_r$ and $(CH_2)_p$ portions of said ring of formula XVI are optionally substituted by 1 to 4 substituents, and the nitrogen atom where X^1 is -NH- is optionally substituted by 1 substituent, said optional substituents being independently selected from the group consisting of $-C(O)O(C_1-C_{10}$ alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, $-NR^7R^8$, C_6-C_{10} aryl, $-S(O)_n(C_1-C_{10}$ alkyl) wherein n is an integer ranging from 0 to 2, and $-SO_2NR^7R^8$;

R^1 is H or C_1-C_{10} alkyl, wherein 1 to 3 carbons of said alkyl are optionally replaced by a heteroatom selected from O, S and N, and said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, -NR^7R^8, C_6-C_{10} aryl, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$;

R^2 is (i) H, R^4, -C(O)R^4, -C(O)OR^4 or -$(CR^7R^8)_mR^3$ when X is -NR^7-, or (ii) H, R^4, or -$(CR^7R^8)_mR^3$ when X is -CR^7R^8-, wherein for both (i) and (ii) m is an integer ranging from 0 to 6 and both R^7 and R^8 may vary for each iteration where m is greater than 1;

each R^3 is independently C_6-C_{10} aryl or 5-10 membered heterocyclyl, wherein said aryl and heterocyclyl groups are optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_6-C_{10} aryl, C_1-C_{10} alkyl, -NR^7R^8, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$; and,

each R^4 and R^5 is independently selected from H and C_1-C_{12} alkyl wherein one or two carbons of said alkyl are optionally replaced be a heteroatom selected from O, S and N, and wherein said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of -C(O)O(C_1-C_{10} alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, C_1-C_{10} alkyl, -NR^7R^8; C_6-C_{10} aryl, 5-10 membered heterocyclyl, -S(O)$_n$(C_1-C_{10} alkyl) wherein n is an integer ranging from 0 to 2, and -$SO_2NR^7R^8$;

R^6 is H, -C(O)R^3 or C_1-C_{18} alkanoyl, wherein in the alkyl portion of said alkanoyl one or two carbons optionally may be replaced by a heteroatom selected from O, S and N; and,

each R^7 and R^8 is independently H or C_1-C_6 alkyl.

2. The compound of claim 1 wherein R^6 is H.

3. The compound of claim 1 wherein X is -NH-.

4. The compound of claim 3 wherein R^2 is H.

5. The compound of claim 1 wherein R^1 is H, benzyl, C_1-C_3 alkyl, or -$CH_2O(CH_2)_2OCH_3$.

6. The compound of claim 3 wherein R^2 is -$(CH_2)_mR^3$ wherein m and R^3 are as defined in claim 1.

7. The compound of claim 6 wherein R^3 is 5-10 membered heterocyclyl.

8. The compound of claim 7 wherein R^3 is quinolin-4-yl, 4-phenyl-1-imidazol-1-yl, imidazo(4,5-b)pyridin-3-yl, 4-pyridin-3-yl-imidazol-1-yl and pyridin-3-yl.

9. The compound of claim 1 wherein said compound is selected from the group consisting of:

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-pyridin-3-yl-imidazol-1-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-pyridin-3-yl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(imidazo(4,5-b)pyridin-3-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(imidazo(4,5-b)pyridin-3-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(7-methoxy-quinolin-4-yl)-propyl))hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(7-methoxy-quinolin-4-yl)-propyl))hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propylidene)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-quinolin-4-yl-propyl)hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-benzoimidazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-benzoimidazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-indazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-carbazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-carbazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(5-phenyl-1H-pyrrol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(5-phenyl-1H-pyrrol-2-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-imidazol-1-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-chlorophenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-chlorophenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-(3-(4-methoxyphenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

19-Deoxo-1-deoxy-5-O-desosaminyl-11-(3-(3-(4-methoxyphenyl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-pyridin-4-yl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-(4-pyridin-4-yl)-(1,2,4)oxadizol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-naphthalen-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-naphthalen-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-benzotrizol-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(1H-indol-3-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(1H-indol-3-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-4-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-4-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-3-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyridin-3-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(pyridin-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(pyridin-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-phenylpropyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-phenylpropyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-bis-(3-phenylpropyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-bis-(3-phenylpropyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-hydroxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-hydroxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(3-methoxyphenyl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(2-phenylethyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(2-phenylethyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(4-phenylbutyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(4-phenylbutyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-furan-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-furan-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-thiophen-2-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-thiophen-2-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrrol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrrol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrazol-1-yl-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-pyrazol-1-yl-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-pyridin-3-yl-thiazol-4-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-pyridin-3-yl-thiazol-4-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-phenyl-thiazol-5-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(2-phenyl-thiazol-5-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-1H-imidazol-2-yl)-propyl)hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-11-(3-(4-phenyl-1H-imidazol-2-yl)-propyl)hydrazo-9-methoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

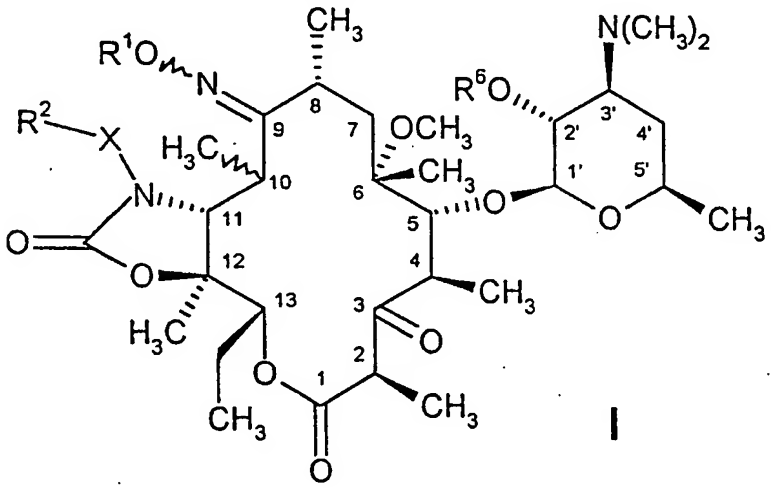
9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-benzoxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate;

9-Deoxo-11-deoxy-5-O-desosaminyl-10-*epi*-11-hydrazo-9-hydroxyimino-6-O-methyl-3-oxoerythronolide A, 11,12-carbamate; and the pharmaceutically acceptable salts of the foregoing compounds.

10. A pharmaceutical composition for the treatment of a bacterial infection or a protozoa infection in a mammal, fish or bird which comprises a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

11. A method of treating a bacterial infection or a protozoa infection in a mammal, fish, or bird which comprises administering to said mammal, fish, or bird a therapeutically effective amount of a compound of claim 1.

12. A method of preparing a compound of the formula



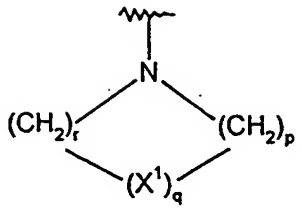
I

or a pharmaceutically acceptable salt thereof, wherein:

X is $-CR^7R^8-$ or $-NR^7-$;

or X is taken together with R^2 to form $-N=CR^4R^5$;

or X and R^2 are taken together to form a heterocyclic ring of the formula XVI:



XVI

wherein in said ring of formula XVI, r and p are each independently an integer ranging from 1 to 3, q is 0 or 1, and X^1 is $-CH_2-$, O, S, -C(O)-, -C(S)-, $-SO_2-$, -CH=CH-, -CH(OH)CH(OH)-, or -NH-; and wherein the $(CH_2)_r$ and $(CH_2)_p$ portions of said ring of formula XVI are optionally substituted by 1 to 4 substituents, and the nitrogen atom where X^1 is -NH- is optionally substituted by 1 substituent, said optional substituents being independently selected from the group consisting of $-C(O)O(C_1-C_{10}$ alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, $-NR^7R^8$, C_6-C_{10} aryl, $-S(O)_n(C_1-C_{10}$ alkyl) wherein n is an integer ranging from 0 to 2, and $-SO_2NR^7R^8$;

R^1 is H or C_1-C_{10} alkyl, wherein 1 to 3 carbons of said alkyl are optionally replaced by a heteroatom selected from O, S and N, and said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of $-C(O)O(C_1-C_{10}$ alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_1-C_{10} alkyl, $-NR^7R^8$, C_6-C_{10} aryl, $-S(O)_n(C_1-C_{10}$ alkyl) wherein n is an integer ranging from 0 to 2, and $-SO_2NR^7R^8$;

R^2 is (i) H, R^4, $-C(O)R^4$, $-C(O)OR^4$ or $-(CR^7R^8)_mR^3$ when X is $-NR^7-$, or (ii) H, R^4, or $-(CR^7R^8)_mR^3$ when X is $-CR^7R^8-$, wherein for both (i) and (ii) m is an integer ranging from 0 to 6 and both R^7 and R^8 may vary where m is greater than 1;

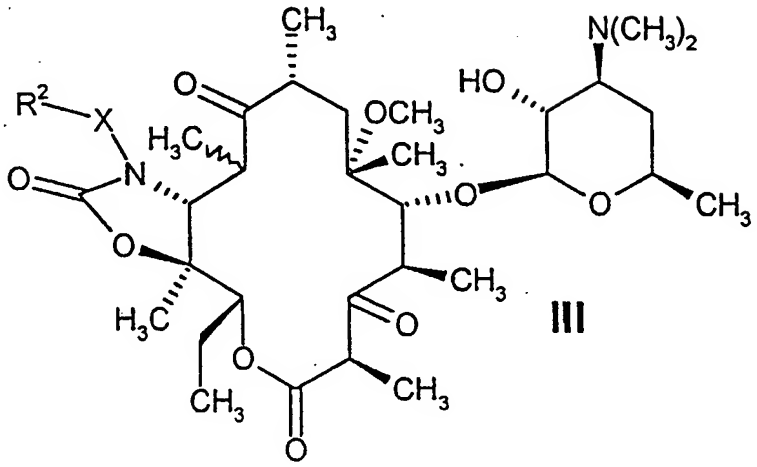
each R^3 is independently C_6-C_{10} aryl or 5-10 membered heterocyclyl, wherein said aryl and heterocyclyl groups are optionally substituted by 1 to 3 substituents independently selected from the group consisting of $-C(O)O(C_1-C_{10}$ alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, 5-10 membered heterocyclyl, C_6-C_{10} aryl, C_1-C_{10} alkyl, $-NR^7R^8$, $-S(O)_n(C_1-C_{10}$ alkyl) wherein n is an integer ranging from 0 to 2, and $-SO_2NR^7R^8$; and,

each R^4 and R^5 is independently selected from H and C_1-C_{12} alkyl wherein one or two carbons of said alkyl are optionally replaced be a heteroatom selected from O, S and N, and wherein said alkyl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of $-C(O)O(C_1-C_{10}$ alkyl), C_1-C_{10} alkoxy, C_1-C_{10} alkanoyl, halo, nitro, cyano, C_1-C_{10} alkyl, $-NR^7R^8$, C_6-C_{10} aryl, 5-10 membered heterocyclyl, $-S(O)_n(C_1-C_{10}$ alkyl) wherein n is an integer ranging from 0 to 2, and $-SO_2NR^7R^8$;

R^6 is H, $-C(O)R^3$ or C_1-C_{18} alkanoyl, wherein in the alkyl portion of said alkanoyl one or two carbons optionally may be replaced by a heteroatom selected from O, S and N; and,

each R^7 and R^8 is independently H or C_1-C_6 alkyl;

which comprises treating a compound of the formula



III

wherein X and R^2 are as defined for said compound of formula I, with a compound of the formula R^1ONH_2•HCl or R^1ONH_2 , wherein R^1 is as defined for said compound of formula I, in the presence of an acid in a polar solvent.

13. The process of claim 12 wherein said solvent is methanol, ethanol, or isopropyl alcohol.

14. The process of claim 12 wherein said acid is Py•HCl, wherein Py is pyridine, or Et_3N•HCl wherein Et is ethyl.

INTERNATIONAL SEARCH REPORT

	National Application No
	PCT/IB 98/00741

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H17/08 A61K31/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 487 411 A (ROUSSEL UCLAF) 27 May 1992 see claim 21	1-14
Y	EP 0 596 802 A (ROUSSEL UCLAF) 11 May 1994 see the whole document	1-14
Y	GB 2 288 174 A (ROUSSEL UCLAF) 11 October 1995 see the whole document	1-14
Y	G. GRIESGRABER ET AL.: "3-Keto-11,12-carbazate Derivatives of 6-O-Methylerythromycin A" J. ANTIBIOT., vol. 49, 1996, pages 465-477, XP002072221 see tables 2-4	1-14

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 July 1998	12/08/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bardili, W

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